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THE JOURNAL

OF THE

American Medical Association

Subscription, $8.00 | PUBLISHED WEEKLY | Single Copies, 25 Cents

VOLUME 117, No. 6 | COPYRIGHT, 1941, BY AMERICAN MEDICAL ASSOCIATION 535 North Dearborn Street, Chicago, Ill. | AUGUST 9, 1941

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Symposium on Treatment of Cancer

Surgical Treatment of Cancer—this is the subject of the Symposium in the August Number (from the Mayo Clinic) of the *Surgical Clinics of North America.* It is a Symposium of special importance—a comprehensive record of today's methods of diagnosing and treating malignancies of the various regions of the body just as these methods are being practiced by the self-same authorities who detail them in this August Number.

There are *20 Clinics* in this Symposium such as: Scope and Importance of the Cancer Problem by Charles W. Mayo; Surgical Treatment of Tumors of the Brain by Alfred W. Adson and George S. Baker; Malignant Lesions of the Thyroid Gland by J. De J. Pemberton and W. R. Lovelace II; Carcinoma of the Breast by Stuart W. Harrington; Results of Treatment of Malignant Lesions of the Stomach by Waltman Walters, Howard K. Gray and James T. Priestley; Carcinoma of the Prostate by Gershom J. Thompson and John L. Emmett; Carcinoma of the Uterus by Virgil S. Counsellor; etc.

Just as this August Number deals with a disease of great importance to all physicians, so does *every number* of the *"Surgical Clinics"* give practical guidance to surgeon and practitioner alike in solving the pressing surgical problems of everyday practice. Thousands of physicians are profiting from these *Books of New Surgery.* Why not start *your* subscription now?

See Also SAUNDERS ADVERTISEMENT on Pages 3, 4, 5

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THE JOURNAL of the American Medical Association is published weekly by the American Medical Association, 535 North Dearborn Street, Chicago, Ill. Subscription price, $8.00 a year. 25c a copy. Canadian $9.50. Foreign $12.00. Entered as second class matter June 25, 1885 at the Postoffice at Chicago, Ill., under Act of March 3, 1879.

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The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 117, No. 6 — COPYRIGHT, 1941, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — AUGUST 9, 1941

THE USE OF SULFANILAMIDE AND SULFATHIAZOLE IN ORTHOPEDIC SURGERY

CHAIRMAN'S ADDRESS

J. ALBERT KEY, M.D.

ST. LOUIS

The discovery that sulfanilamide in low concentrations which are tolerated in the animal body inhibits the growth of certain pathogenic bacteria has led to the use of this drug in the treatment of a wide variety of conditions. It has also stimulated experimental studies of the effects of the drug on various pathogenic organisms and on the animal body. As sulfanilamide is moderately toxic and affects only certain bacteria, a large number of related compounds have been synthesized and are being studied. The most widely used are sulfanilamide, sulfapyridine and sulfathiazole. It is possible that sulfadiazine may be added to this list (Feinstone and others,[1] Long [2]).

Since sulfapyridine is particularly effective against the pneumococcus and is not more active against pyogenic organisms than are the other two drugs mentioned, orthopedic surgeons are not particularly interested in it.

In this paper I shall consider especially the use of sulfanilamide and sulfathiazole in orthopedic surgery. It is now generally recognized not only that sulfanilamide is a valuable drug when administered by mouth or through other routes for its bacteriostatic effect on bacteria which may be present in the animal body but also that it is useful when implanted locally in contaminated or infected wounds. The same fact is true of sulfathiazole, though this is not yet generally recognized. Sulfanilamide is effective against hemolytic streptococci in low concentrations but has relatively little effect on staphylococci or Clostridium welchii unless the drug is present in a very high concentration. Sulfathiazole is as effective against streptococci as is sulfanilamide and is more effective against staphylococci, Clostridium welchii and Clostridium septique but is not effective against Clostridium oedematiens (Hawking [3]). However, a good deal more data are needed on its experimental and clinical use in staphylococcic infections and gas gangrene before sulfathiazole can be properly evaluated. It is much less soluble than sulfanilamide and consequently may be expected to remain in the wound longer after local implantation. On the other hand, the concentration of sulfathiazole in the fluid in the wound will be much less than will that of sulfanilamide under the same conditions. More work is needed on the effect of saturated solutions of these drugs on pathogenic bacteria.

The local use of these drugs has for its rationale the fact that the fluid which is present in the wound becomes temporarily saturated with the drug and that a local concentration can be obtained which is many times higher than that present in the blood after full therapeutic doses. Since the effectiveness of the drug varies directly with the concentration, the advantage of a high local concentration in the area where the bacteria are is obvious.

It has been shown that a saturated solution of sulfanilamide or the implantation of the powder in a wound does not seriously damage tissues or seriously interfere with wound healing, and experiments in progress indicate that the same statement is true of sulfathiazole (Key and others [4]).

It has also been demonstrated that sulfanilamide can be used locally in suitable amounts in operative wounds without danger of serious toxic effects (Key and Burford [5]) and I believe that I now have had sufficient experience with sulfathiazole to indicate that the same statement is true of this drug.

It is further to be noted that these drugs are dissolved independently by the solute. That is, if one drug is added to a saturated solution of the other drug, it too will be dissolved in the usual amount; thus the fluid may be saturated with the two drugs at the same time. I believe that this is important and I am now using mixtures of sulfanilamide and sulfathiazole powder in both clean and infected wounds. The mixtures are tolerated by the tissues and do not seem to interfere with the healing of the wounds, but it is too early yet to state whether or not they are more effective bacteriostatic agents than are the single drugs.

CLINICAL USE

In considering the clinical use of these drugs in orthopedic surgery it seems advisable to divide the patients into the following groups: patients with (1) clean operative wounds, (2) contaminated traumatic wounds, (3) acute pyogenic infections and (4) chronic pyogenic infections.

1. *Clean Operative Wounds.*—In reports on the local implantation of sulfonamides in experimental animals it was stated that sulfanilamide was being used

From the Department of Surgery of the Washington University School of Medicine.

Read before the Section on Orthopedic Surgery at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Feinstone, W. H.; Williams, R. D.; Wolff, R. T.; Huntington, Evelyn, and Crossley, M. L.: The Toxicity, Absorption and Chemotherapeutic Activity of 2-Sulfanilamidopyrimidine (Sulfadiazine), Bull. Johns Hopkins Hosp. **67**: 427 (Dec.) 1940.

2. Long, P. H.: Sulfadiazine: The 2-Sulfanilamidopyrimidine Analogue of Sulfanilamide, J. A. M. A. **116**: 2399 (May 24) 1941.

3. Hawking, Frank: Prevention of Gas Gangene Infections in Experimental Wounds by Local Application of Sulfonamide Compounds and by Sera, Brit. M. J. **1**: 263 (Feb. 22) 1941.

4. Key, J. A.; Frankel, C. J., and Burford, T. H.: The Local Use of Sulfanilamide in Various Tissues, J. Bone & Joint Surg. **22**: 952 (Oct.) 1940. Key, J. A., and Frankel, C. J.: The Local Use of Sulfanilamide, Sulfapyridine and Sulfamethylthiazole, Ann. Surg. **113**: 284 (Feb.) 1941.

5. Key, J. A., and Burford, T. H.: The Prophylactic Implantation of Sulfanilamide in Clean Operative Wounds for the Reduction of Postoperative Infection, to be published.

locally and not only in contaminated and infected wounds but also in clean operative wounds.[4]

The routine use of the sterile dry powder of one of the sulfonamide drugs in all clean operative wounds during the past two years has confirmed the value of the procedure and has led me to believe that for orthopedic surgeons this affords the widest field of usefulness for these preparations. During this period I have used sulfanilamide in 150 cases,[5] sulfathiazole (in sterile ampules supplied by the Abbott Laboratories) in 70, and a mixture of sulfathiazole and of sulfanilamide (supplied by Hynson, Westcott and Dunning) in 23. In none of these has a postoperative infection occurred. This series represents a good many more wounds than patients, because many of the patients had two or more separate incisions.

Under the best of operative conditions a certain percentage of postoperative infections is unavoidable. Since this is true and since one is not able to determine beforehand which wounds will become infected, it must be admitted that every so-called clean operative wound is potentially an infected wound. If, in addition to using every precaution to prevent operative infection, one can place within the wound a sterile substance which will prevent the growth of any casual bacteria which may have gotten into the wound through an accidental break in operative technic or from the surrounding air and at the same time know that this substance will not seriously injure the patient or interfere with the healing of the wound, it seems reasonable to use this substance.

The experience with 243 cases demonstrates that sterile sulfanilamide and sulfathiazole are suitable substances for implantation in clean operative wounds and that their use in this manner tends to lessen the incidence of postoperative infections. In this series there has not been any appreciable interference with the healing of the wounds. In a few of the early cases in which too much of the drug was placed in small wounds there was a tendency to the accumulation of an excess amount of serum in the wound and in 2 cases this serum was expressed after the sutures were removed. In neither instance, however, was there any evidence of infection, and the wounds healed by primary intention except for the small area left open after the expression of the serum, and here the healing was delayed for a few days. During the past year and a half there have been no such instances, as during this time the amount of the drug used has been relatively small—rarely over 5 Gm. in one operative wound and in many instances only 1 or 2 Gm. or even less in small wounds, the object being not to place enough of the powder in the wound to interfere with the coaptation of the wound surfaces or to permit the formation of aggregates in the depth of the wound. One patient developed a bed sore which interfered with the healing of a spinal fusion wound, but this was due to poor postoperative care and not to the use of the drug.

The next question that arises is whether or not the local implantation of the drug tends to cause toxic symptoms in the patients. In certain instances there was an unexplained elevation of temperature after the operation. This occurred in 7 cases of the sulfanilamide series. It has seemed to be somewhat more frequent with the use of sulfathiazole than with sulfanilamide, but the data on this series are not yet complete. In no instance did the rise of temperature last more than a few days, nor did it do any harm other than cause anxiety to the surgeon. There was no other evidence of toxicity in cases in which the drug has been used locally in clean operative wounds. Three patients had a rash after the operation, but 2 of these were patients with chronic osteomyelitis who were also taking the drug by mouth. The third was a small child who had a relatively large amount of sulfanilamide implanted in a tuberculous cavity in the ilium. It is thus evident that the drug can be used locally in clean operative wounds with safety.

The rationale of the procedure is that by the use of the drug in this manner a high concentration—that is, a saturated solution—of the drug is brought into direct contact with any organisms which may be present in the wound. This concentration of the drug in the wound lasts approximately forty-eight hours—that is, until the drug is absorbed and excreted. It is probable that the sulfathiazole lasts longer. The time during which the drug remains in the wound will vary directly with the amount implanted and indirectly with the blood supply of the area and with the surface exposed for absorption. In tissues well supplied with blood the absorption is more rapid than it is in areas where the blood supply is scanty. It can be placed in joints and other body cavities and apparently does no harm to the lining of these cavities. However, it is to be noted that in large cavities, such as the peritoneum or the pleura, an extensive surface is exposed to the drug and consequently the absorption may be unusually rapid and cause high concentrations of the drug in the blood. For this reason it seems advisable to use a mixture of sulfanilamide and the less soluble sulfathiazole in these cavities.

In addition to placing the powder in the wound before it is sutured, a small amount is sprinkled along the suture line after the skin is closed. The dressing is then put on and the drug will tend to saturate the blood or serum which drains from the wound and thus prevent the development of stitch abscesses. This is especially true if the wound is encased in a plaster of paris cast in which it is undesirable to change the dressing for some time.

It is to be emphasized that the use of the drug in the wound for the prevention of infection does not warrant any letting down in surgical technic, because it is not infallible and I know of 4 instances in which postoperative infections have occurred after sulfanilamide powder has been placed in so-called clean wounds.

2. *Contaminated Traumatic Wounds.*—These are lacerations or compound fractures which are treated before sufficient time has elapsed after the injury to permit the development of an actual infection in the tissues. In civilian life it is usually stated that a wound is not considered infected until from six to twelve hours after the injury, the time varying inversely with the amount of damage to the tissues; that is, in a wound with relatively little damage to the issues a greater amount of time will elapse before actual infection develops, other things being equal.

There is considerable difference of opinion as to whether or not such wounds should be sutured. It has been my custom to close such wounds by primary suture after a careful débridement and expect primary healing. If I was not satisfied that I had done an adequate débridement and removed all devitalized tissue and foreign material in the wound, it was packed open with petrolatum gauze. This method has been used for the last twenty years and most such wounds have been sutured immediately with satisfactory results. By the use of sulfanilamide or sulfathiazole powder in the wound, or a mixture of the two, a wound can be sutured

with more assurance than could the same wound without the use of the powder (Key[6]). In other words, the powder will tend to keep down the infection until the clearing mechanism of the body has had a chance to eliminate the bacteria. That most compound fractures in civilian life can be debrided and sutured primarily with satisfactory results if sulfanilamide powder is implanted in the wound is amply proved by the series of such cases reported by Jensen, Johnsrud and Nelson[7] and by Jackson.[8]

If one believes that these wounds should not be sutured after débridement but should be left open and the wound packed with petrolatum gauze or with other material, in order to permit drainage, then the probably mild infection which will eventually develop on the surface of the wound will be minimized by sprinkling the powder over the surface of the wound before the petrolatum gauze or other packing material is inserted.

The use of sulfanilamide or sulfathiazole in the wound does not permit the letting down of any of the standards for a complete débridement of the wound, nor does it eliminate the necessity for adequate reduction of the fracture and immobilization of the part after the wound has been sutured or after the wound has been packed open. It does, however, permit the use of internal fixation in the treatment of compound fractures.

In military surgery, which is occupying such a prominent place in our thoughts, the use of sulfanilamide or sulfathiazole powder or a mixture of the two will lessen the incidence of infection after wounds have been debrided. However, contaminated war wounds should not be sutured, and especially is this true in a war of movement where the men are treated in casualty clearing stations or other hospitals and are then moved on after a few hours or after a longer interval.

When a surgeon debrides and sutures a contaminated wound he should assume the obligation of watching this patient until the danger of infection has passed. For this reason it is not wise to advocate débridement and immediate closure of war wounds in military surgery. Many of these will have to be left open, not because they could not have been sutured under favorable conditions but because it is not possible to keep the patients in the hospital and under the care of the operating surgeon until sufficient time has elapsed so that the danger of infection is no longer present. It is further to be noted that the transportation of such patients either in casts or in splints causes a variable amount of movement of the part and exposure of the patient and is accompanied by some pain. Movement of the part lowers the local resistance, and pain and exposure lower the general resistance. Consequently, transportation of a recently operated compound fracture tends to favor the development of an infection in the wound.

In civilian life the movement of the part, pain and exposure can be reduced to a minimum, but under war conditions, and especially those of total war, military necessity may cause the wounded who have recently been operated on to be transported when and if the opportunity presents itself and by whatever means are available. Consequently, wounds in war should be debrided, sprinkled liberally with sulfanilamide or sulfathiazole or, preferably, a mixture of the two, packed open with petrolatum or plain gauze and immobilized in a cast or splint which will maintain the reduction effected during the operation.

The question immediately arises as to whether or not these men should also be given sulfanilamide or sulfathiazole by mouth. Ordinarily in civilian practice I do not give sulfanilamide or sulfathiazole by mouth to a patient with a recently debrided and sutured contaminated wound. It is believed that adequate débridement plus local implantation of the drug are sufficient and this has been my experience in the past. On the other hand, in certain cases in which a little more time than is considered safe has elapsed or I am not quite sure of the efficiency of the débridement, in addition to placing the drug in the wound I give the patient full doses of sulfathiazole by mouth before the operation and as soon as he is able to take it after the operation (usually 2 Gm. is given before the operation and 1 Gm. every four hours for the first two days after the operation). If there is no evidence of infection at the end of two days the drug is stopped entirely, or it may be tapered off. Fluids are forced while sulfathiazole is being given in order to prevent damage to the kidneys. This plan seems suitable for war wounds, in which the danger of infection is greater than in civil life.

3. *Acute Pyogenic Infection.*—These patients fall into two groups: (1) those with contaminated wounds in which sufficient time has elapsed to permit the development of infection and (2) acute hematogenous pyogenic infections, such as acute osteomyelitis and acute arthritis.

In the first group the wound, usually a compound fracture, is open and is draining but the drainage is inadequate. There is usually a mixed infection, and the bacteria are not all on the surface of the wound but have grown into the tissues, and the organisms of gas gangrene may be present. These patients are ill with a systemic infection and need the drug which will most effectively combat a mixed infection. This is sulfathiazole, and it should be given by mouth in full doses or, if necessary, as the sodium salt intramuscularly in strong solutions or intravenously in dilute solutions.

In addition to the general administration of the drug, the wound should be adequately drained, foreign bodies should be removed and obviously devitalized tissue should be excised. All acutely infected wounds should be left wide open. In gas gangrene, involved muscle should be excised and the patient should be given large doses of the polyvalent serum.

After the operation is completed and the toilet of the wound is made, the surface of the wound and its depths should be sprinkled liberally with sulfathiazole or with a mixture of sulfathiazole and sulfanilamide, the amount of the drug being considerably more than is used in wounds which are being closed. This is for two reasons. The first is that absorption of the drug will be less and the second is that with an established infection it is probable that large numbers of bacteria will remain in the tissues even after an adequate débridement.

Finally, the wound should be immobilized and the patient should receive supportive treatment, including a transfusion of blood or plasma if indicated, and the sulfathiazole should be continued by mouth until evidence of general infection has subsided.

In hematogenous pyogenic osteomyelitis or pyogenic arthritis the problem is somewhat similar, except that the focus of the infection has not been drained. At the present time there is considerable difference of opinion as to whether or not this local focus should be attacked

6. Key, J. A.: Treatment of Compound Fractures, Nebraska M. J. **24**: 367 (Oct.) 1939.
7. Jensen, N. K.; Johnsrud, L. W., and Nelson, M. C.: Local Implantation of Sulfanilamide in Compound Fractures, Surgery **6**: 1 (July) 1939.
8. Jackson, Ruth: A Comparative Study of the Treatment of Compound Fractures, South. M. J. **34**: 319 (March) 1941.

surgically. Many believe that acute hematogenous osteomyelitis is a general disease or septicemia of which the local focus in the bone is but one manifestation, and that the patient should be treated medically rather than surgically. I do not concur in this belief. It is my opinion that the local infection in the bone should be drained as soon as it is safe to do so; that is, as soon as the patient is in condition to stand the operation.[9]

The chemotherapeutic agents at our command cannot be relied on to sterilize an abscess cavity in the bone when they are administered by mouth. It is true that when sulfanilamide or sulfathiazole is given by mouth a concentration is eventually obtained in the fluid of the abscess cavity which approaches that present in the blood. In my experience the concentration obtained in the pus has been approximately 50 per cent of that present in the blood. However, this concentration is not sufficient to kill staphylococci.

There is no doubt that in certain cases of acute pyogenic osteomyelitis, if large doses of sulfathiazole are given, the disease in the bone will subside and the bone will eventually heal. How frequent these cases are, I do not know. I have seen 1. On the other hand, I have seen patients who developed metastatic foci while they were receiving full doses of sufathiazole and who eventually became osteomyelitic derelicts as a result of widespread destruction of bones and joints. Other patients have died without operation. I have also seen patients with mild pyogenic infections in bone get well without surgical intervention or chemotherapy.

Sulfathiazole rather than sulfanilamide should be used in every case of acute pyogenic osteomyelitis. It should be given in full doses by mouth if possible or intramuscularly or intravenously if necessary. As soon as the patient is in condition for the operation, the focus in the bone should be drained. No attempt should be made to remove the entire area of the disease. At the operation sulfathiazole powder or a mixture of sulfanilamide and sulfathiazole should be implanted in the wound in liberal amounts. The wound should then be packed loosely with petrolatum gauze and the extremity immobilized in a plaster cast. Supportive treatment of the patient should be continued and the patient should be given full doses of sufathiazole by mouth until his temperature has subsided. At the same time fluids should be forced. For a very toxic patient the staphylococcus antitoxin should be used if it is available. The drug will exert a favorable influence on the septicemia, lower the mortality, tend to decrease the amount of destruction of bone and decrease the number of metastatic foci which tend to develop in this disease.

The same is true of acute pyogenic arthritis. The joint should be opened, washed out with physiologic solution of sodium chloride, a liberal amount of sulfathiazole powder should be implanted in the joint cavity and, as a rule, the joint should be left open. In certain relatively mild infections I have closed the joint and immobilized it, and the wounds have stayed healed and a useful joint has resulted.

4. *Chronic Pyogenic Infections.* — These include chronic osteomyelitis and chronic infections of soft tissues, either deep infections or surface infections. As staphylococci are usually present, sulfathiazole is the drug of choice, although sulfanilamide powder in concentrated form will tend to lessen the amount of drainage and decrease the activity of the infection in the wound. Either drug is useful as a dusting powder for chronic surface infections and tends to lessen the amount of secretion in chronic osteomyelitis. But they cannot be expected to cure chronic infection in bone. The same fact is true of sulfathiazole by mouth in chronic osteomyelitis. In certain instances in which the condition is nonoperable, as in extensive involvement of the shaft of the femur, I have given patients the drug by mouth over a considerable period and they have felt better and the discharge from the wound has been less. None of these infections, in my experience, have healed and remained healed. The chief use of the drug in chronic osteomyelitis is that recently pointed out by Dickson and Diveley.[10] They have shown that chronic osteomyelitis can be treated surgically and the wound can then be sprinkled with sulfathiazole powder and closed.

I have followed this procedure in 17 cases and in none of these have there been any untoward results. Fourteen healed by primary intention. In the 3 others there was a definite reason for the failure of primary healing. One of these was an extensive disease of the tibia in which, after sequestrectomy and saucerization, it was not possible to close the wound completely. It eventually healed by granulation. Another tibia was operated on eight weeks after the acute focus in the bone had been drained. This was cleaned out thoroughly and the wound was almost closed. This wound is now healed. In the third case, in which operation was performed four weeks after the onset, a large abscess was drained, the femur was opened and extensive necrosis was present in the lower end of the shaft. The drug was given by mouth as well as locally, and the wound was packed open. There had been extensive destruction of bone, and this child may require a second operation for the removal of a sequestrum.

The operation is most successful in chronic osteomyelitis in which sinuses can be excised, all dead bone can be removed and the walls of the wound can be closed. For one or two days before the operation the patient is given full doses of sulfathiazole by mouth—that is, 1 Gm. every four or six hours—and this is continued after the operation until danger of a flare-up of the infection is past, usually only for three or four days. The dose is then gradually tapered off.

In operating in such cases I have not used any deep sutures but have closed only the skin and fascia with large through and through sutures of silkworm gut. After the operation the limb is immobilized in a plaster of paris cast without drainage. When the drug is being given by mouth toxic manifestations are more apt to occur, and in 2 of the 17 cases a rash developed after the operation.

CONCLUSIONS

1. The implantation of sterile sulfanilamide or sulfathiazole powder in clean operative wounds is a safe procedure and will decrease the incidence of postoperative infections.

2. The local use of the drug will lessen the incidence and severity of infection in contaminated wounds whether these are sutured or left open.

3. Acute pyogenic infections should be drained adequately, and sulfathiazole should be used locally and given by mouth in full doses.

4. Chronic pyogenic foci in bone and soft tissues can be excised and the wound closed if sulfathiazole is given in full doses by mouth and implanted in the wound before it is sutured.

9. Key, J. A.: The Early Operative Treatment of Acute Hematogenous Osteomyelitis, Surgery **9**: 657 (May) 1941.

10. Dickson, F. D., and Diveley, R. L.: The Treatment of Chronic Osteomyelitis with Sulfathiazole, to be published.

ROCKY MOUNTAIN SPOTTED FEVER

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Rocky Mountain spotted fever is an acute infectious disease caused by the virus-like organism Dermacentroxenus rickettsii, which is transmitted to human beings by an infected tick. The infection is characterized clinically by an acute onset with chills and fever, severe headache, restlessness, delirium and a characteristic hemorrhagic eruption of the skin. The histopathologic picture of the early stage of this cutaneous manifestation is a proliferation of the endothelial lining of the small blood vessels followed by necrosis of the endothelium and of the smooth muscle of the media. Later, typical manifestations of phlebitis, thrombosis and gangrene may be present.

DISTRIBUTION AND CARRIERS

Rocky Mountain spotted fever, recognized for half a century in the Rocky Mountain states, can no longer be considered as limited in distribution to the Rocky Mountain states area because the *Public Health Reports* [1] show a total of 2,190 cases occurring in thirty-seven of the forty-eight states during the five year period from 1933 to 1937 inclusive, 1,435 cases, or 65.5 per cent, occurring in the Mountain and Pacific states, and 601 cases, or 27.4 per cent, occurring in the South Atlantic group. These two areas accounted for 93 per cent of the total number of reported cases. The occurrence of the infection is seasonal and the human infections occur during the tick season. The western type, of which the carrier is the wood tick, occurs in the spring, with the majority of cases in the months of April and May. The eastern type, of which the carrier is the dog tick or the rabbit tick, has a longer season running through spring, summer and autumn.

Wilson and Chowning [2] in 1902 suggested that Rocky Mountain spotted fever was transmitted by the wood tick Dermacentor andersoni and that an animal reservoir existed somewhere in nature. Ricketts [3] in 1906 demonstrated the presence of infected wood ticks in nature and the hereditary passage of the infectious organism from one generation of ticks to the next. McColla [4] in 1908 published the results of an experiment in which, three years previously, he removed a wood tick from a patient showing early symptoms of Rocky Mountain spotted fever and produced the disease in two volunteers by allowing this tick to feed on them. Maver [5] in 1911 suggested that the American dog tick Dermacentor variabilis could transmit Rocky Mountain spotted fever, and this observation was proved in 1931 by the work of Rumreich, Dyer and Badger.[6] From the result of field observations in 1917, Badger demonstrated in 1923 that the rabbit tick Haemaphysalis leporis palustris Pack can be a carrier. Parker [7] has found five other species of ticks in the United States that under laboratory conditions are potential carriers of Rocky Mountain spotted fever.

CAUSATIVE ORGANISM

Human infections with Rocky Mountain spotted fever are acquired only through the medium of infected ticks, usually by tick bites. There is no characteristic lesion at the site of attachment of the tick, and not infrequently the site of the bite cannot be found. If a lesion not due to irritation is present it is likely the result of secondary infection or some tick-borne agent other than the spotted fever rickettsia. Occasionally there is enlargement of the regional lymph nodes. Some few human infections are probably contracted through the skin without a tick bite by contamination with tissues of infected ticks resulting from picking ticks from domestic animals with the bare hands.

The causative agent of Rocky Mountain spotted fever is a gram-negative staining bacillus, Dermacentroxenus rickettsii. The known characteristics of this microorganism seem to indicate that it is intermediate between a bacterium and a filtrable virus, that it can be cultivated only in vivo and that it can be demonstrated in stained sections of infected tissues. Further research work is necessary to establish the method of transfer of this infectious agent from one generation of tick to another.

The terms "eastern type" and "western type" of Rocky Mountain spotted fever are frequently used in the literature. To some persons, at least, this differentiation has seemed to rest mainly on the false assumption that the disease in the West is consistently characterized by a higher case fatality rate than in the East. Evidence that the eastern type is not always a mild infection is clearly demonstrated by the considerable number of reported cases in which the diagnosis has been established post mortem. The differentiation between the two types is perhaps more accurately defined by assuming that the western type occurs in areas which are the habitat of the wood tick while the eastern type occurs outside of these areas, the infection being carried by a different species of tick.

Parker has shown that the virus of any individual Rocky Mountain wood tick of a local tick population may range in virulence from a nonimmunizing nondemonstrable phase to that of the prevailing maximum local virulence.

In a fasting, hibernating Rocky Mountain wood tick or one just emerging from hibernation, the virus is usually either completely inactive or in a phase which causes inapparent infections when injected into laboratory animals. However, if such a tick is incubated or is allowed to ingest blood, the virus becomes "reactivated" and soon reaches its maximum potential virulence.

The variation of the virus together with a demonstrable difference in individual resistance or susceptibility to the infection is a definite factor in the production of the three differentiated clinical types of Rocky Mountain spotted fever: the mild type, the severe type and the fulminating type.

CASES OF MILD TYPE

The group of cases of mild type, including a far greater number of infections than the other two groups combined, is composed of the cases ranging in severity from those presenting symptoms and clinical signs sufficient only for a positive diagnosis to those in which

Read before the Section on Dermatology and Syphilology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Hampton, B. C., and Eubank, H. G.: Rocky Mountain Spotted Fever, Pub. Health Rep. **53**: 984-990 (June 17) 1938.
2. Wilson, L. B., and Chowning, W. M.: Reports on the Investigation of So-Called Spotted Fever, First Biennial Report of Montana State Board of Health, 1903, p. 27.
3. Ricketts, H. T.: Contributions to Medical Science, Chicago, University of Chicago Press, 1911.
4. McColla, L. P.: M. Sentinel **16**: 87, 1908.
5. Maver, M. B.: Transmission of Spotted Fever by the Tick in Nature, J. Infect. Dis. **8**: 327, 1911.
6. Dyer, R. E.; Rumreich, A. S., and Badger, L. F.: Typhus-Rocky Mountain Spotted Fever Group in United States, J. A. M. A. **97**: 589 (Aug. 29) 1931.
7. Parker, R. R.: Certain Phases of the Problem of Rocky Mountain Spotted Fever, Arch. Path. **15**: 398 (March) 1933.

there is moderate sickness and toxicity, with the temperature remaining under 102.5 F. and the pulse rate not exceeding 90 a minute.

The incubation period of the cases of mild involvement is from three to fourteen days. There is usually a prodromal period of two or three days characterized by loss of appetite, irritability, malaise and chilly sensations.

The typical cases start with a chill and a rather slowly rising temperature reaching its peak on the fifth day. The complaints are of a severe basal and frontal headache and pains in the muscles, bones and joints. Restlessness and insomnia are usually well defined, and some degree of cyanosis is present.

The characteristic cutaneous lesions appear usually on the fourth to the sixth day, accompanied by a decrease in the severity of the muscular pains. The eruption consists of bright red, widely scattered maculopapular lesions which at first will disappear on pressure. Later they become darker, enlarge by peripheral extension and will not disappear on pressure. After three or four days there is usually another "crop" of lesions and not infrequently as many as three distinct "crops" are seen in a case of mild involvement. The cutaneous lesions then undergo the changes seen in extravasation of blood into cutaneous tissue, with the pigmentation remaining in these areas for several weeks or even months.

The temperature after reaching its peak usually remains rather constant until the beginning of the third week, at which time it falls by lysis, which usually requires a period of six to eight days in the western type and from three to four days in the eastern type of infection.

CASES OF THE SEVERE TYPE

In cases of severe involvement the incubation period is from two to five days and the onset is sudden, being ushered in with a hard chill and presenting some combination of the following symptoms: malaise, sweating, severe backache, frontal and occipital headache, injection of the conjunctivas, sensitivity of the eyes to pressure, photophobia, pain in the muscles, bones and joints, nosebleed, nausea, aphasia and lack of muscular coordination. The severity of the symptoms increases rapidly and the face soon assumes a dusky flush.

The temperature rises steadily until by the third day it has reached 103 or 104 F., which ordinarily is the peak except for fatal cases, in which not uncommonly terminal hyperpyrexia of 106 F. or higher develop. The elevation of temperature is accompanied by an increase in pulse rate from 110 to 140 a minute. The mind may remain unusually clear, but more often there is a stupor from which the patient is easily aroused.

The cutaneous rash usually appears on the second or third day as a bright red generalized macular eruption on areas including the palms of the hands, the soles of the feet, the scalp and quite frequently the mucous membrane of the mouth and throat. These maçules soon become a darker hue and will not disappear on pressure. They enlarge by peripheral extension and coalesce to form confluent hemorrhagic blotches which for several months after recovery remain as pigmented areas. The course of the febrile period is exceedingly stormy and the period of convalescence for the survivors is usually from several to many months, and even then a considerable percentage fail to regain a condition comparable to their previous normal state of health. The acute symptoms ordinarily last for three weeks or longer, with the temperature falling by lysis and requiring a period of a week or ten days to regain a normal level.

CASES OF THE FULMINATING TYPE

Cases of the fulminating type start suddenly with a chill followed by a rapid rise in temperature and an increase in the pulse rate. The symptoms are more severe, especially those of the nervous system, than in the severe type with more evidence of a profound toxicity. Incontinence of urine and feces, convulsions, muscular tremors, muscular rigidity and opisthotonos are commonly seen. The cutaneous manifestation, which at first is composed of closely spaced macular lesions, spreads rapidly and becomes a confluent hemorrhagic eruption with necrosis and sloughing, the parts commonly affected being the scrotum, prepuce, vulva, soft palate and dependent portions of the body and buttocks. The course of the disease in these cases is exceedingly rapid, with the patient lapsing into a profound coma and the temperature continuing to rise to a high level, with death occurring as the result of an overwhelming toxicity accompanying an extremely virulent infection.

MANIFESTATIONS AND COMPLICATIONS

Common clinical signs, in addition to those which have been mentioned, are enlargement of the spleen, enlargement of the liver and jaundice. Laboratory examinations show a concentration of the urine, commonly with albuminuria. The white blood cell count does not usually exceed 15,000 but may be 30,000. The red blood cell count may be below or slightly above normal. The spinal fluid is normal.

Fatalities rarely occur in the cases of mild involvement, are fairly common in the cases of severe involvement and are the usual termination in cases of the fulminating type of Rocky Mountain spotted fever. Death, however, may occur in any of the types from complications or from concurrent conditions. The most common complications are pneumonia, phlebitis, hiccups, hemorrhage from the nose, intestine or kidneys, with iritis, acute nephritis and hemiplegia appearing less frequently. The concurrent conditions, due directly or indirectly to ticks, that may occur are streptococcic septicemia, tularemia and tick paralysis.

The *Public Health Reports* showed 233 deaths among 1,203 cases occurring in the Western states from 1933 to 1936 inclusive, which is a fatality rate of 19.4 deaths per hundred cases. The South Atlantic states reported during the same period 86 deaths among 469 cases, or a case fatality rate of 18.1 deaths per hundred cases.

DIAGNOSIS

The clinical diagnosis of Rocky Mountain spotted fever is often difficult even for those familiar with the disease. Particularly is this true of the very mild attacks and of the rapidly fatal attacks of the fulminating type. Certain cases of toxoplasmosis have been reported to exhibit cutaneous manifestations closely resembling the cutaneous eruption of Rocky Mountain spotted fever. Another problem in diagnosis is presented when Rocky Mountain spotted fever occurs in an area in which typhus fever is endemic. For these reasons, if at all feasible, a clinical diagnosis of Rocky Mountain spotted fever should be confirmed by one or more laboratory tests. The three tests ordinarily used are the infection test, the Weil-Felix reaction and the protection or virus-neutralization tests. However, a description of these tests is not within the scope of this paper. In the cases with a fatal outcome additional confirmation of clinical diagnosis can be obtained by demonstration of the characteristic pathologic changes in diseased tissue.

TREATMENT

At present no drug has been found that exerts any specificity toward the infectious organism of Rocky Mountain spotted fever. The best treatment is symptomatic and supportive. Conservative treatment seems to be the most successful. Early hospitalization and adequate nursing care are considered the most important items to spare the patient every possible exertion. Elimination should be promoted by frequent enemas, and the fever should be reduced by sponge baths and alcohol rubs. Dehydration should be prevented by forcing liquids orally, rectally, subcutaneously or intravenously. Codeine is the drug of choice for restlessness and insomnia. Convalescent serum and transfusions from immune or nonimmune persons have shown no definite specificity in this infection.

PROPHYLAXIS

The United States Public Health Service vaccine for Rocky Mountain spotted fever is prepared at the Rocky Mountain Laboratory of the National Institute of Health at Hamilton, Mont.

The vaccine is given in two doses of 2 cc. each at an interval of five days, either subcutaneously or intramuscularly. The known data indicate that the vaccine fully protects the majority of persons against the less virulent strains but that the average person is only partially protected against the highly fatal type of Rocky Mountain spotted fever, and that the maximum degree of protection conferred is retained for less than one year.

REPORT OF CASES

CASE 1.—A white woman aged 23, admitted to Colorado General Hospital on May 31, 1940, complained of chills, fever and headache for one week and rash for three days. On May 19 the patient discovered a tick attached to the skin of her abdomen. The tick was removed the following day. May 24 the patient had a severe chill, followed by an elevation of temperature to 105.8 F.; since that time she had had continuous fever, the minimum having been 100 F. On May 28 a maculopapular rash appeared, first on her arms and legs, with subsequent crops involving the trunk, palms of the hands and soles of the feet. Past illnesses consisted of cystitis at 5 years, scarlet fever at 12 years and measles at 10 years. She had had a fever of undetermined origin in 1936 and staphylococcic septicemia in 1937; tonsillectomy had been performed at the age of 12 years. The remainder of the history was inconsequential. Examination on admission revealed a temperature of 102.4 F., a pulse rate of 80 and a respiratory rate of 20. The patient was well developed and well nourished; she was in no apparent distress but appeared toxic. The skin of the entire body, including the palms of the hands and the soles of the feet, showed a discrete, rather sparsely situated erythematous maculopapular rash which faded on pressure. Examination of the abdomen gave negative results except for a palpable spleen. In the right inguinal region was a small healed area immediately over a swollen lymph node; this was stated to be the area of the initial tick bite. The urine on admission was normal. Examination of the blood showed hemoglobin 12.5 per cent, red cells 3,830,000, white cells 9,800 with 81 per cent polymorphonuclear leukocytes, 14 per cent lymphocytes and 5 per cent endothelial cells. The polymorphonuclear leukocytes were young and granular. The sedimentation rate was 2 per cent in one-half hour and 3.5 per cent in one hour. Serologic examination gave negative results. The blood chemistry was normal. An agglutination test for Bacillus abortus and Widal tests were negative on June 3. Blood cultures taken on May 30 and 31 and June 2 were consistently negative at three days. Culture of the urine was negative. Culture of the feces was not contributory. The patient was treated conservatively and given acetylsalicylic acid and cold sponges for high temperature and sedation. The urine on June 3 and 7 continued to be normal. Blood counts remained about the same throughout her entire hospital course. The patient averaged three chills a day, her temperature rising from 100 to 105 F. for four days. She appeared acutely ill and the eruption became much more severe and more confluent. By June 3 the lesions were hemorrhagic and thickest about the wrists and ankles. The Weil-Felix reaction on June 5 was negative and on June 11 positive in dilutions of 1:50 to 1:200. Sulfapyridine therapy was instituted on June 3 with a view to preventing the chills and high fever. The temperature immediately fell and the patient appeared to improve clinically, with healing of the tick bite and disappearance of the adenopathy. By June 10 the temperature reached normal and remained so. The remainder of the hospital course was satisfactory, the eruption faded gradually and the patient was discharged June 14.

CASE 2.—A man aged 44 entered Presbyterian Hospital May 22, 1940 as a patient of Dr. Charles Jaeger. The patient had gone on a fishing trip over the week end of May 18 and after returning home on Sunday the 19th discovered a tick attached to the skin of the abdomen below and to the right of the umbilicus. The tick was removed Sunday evening by Dr. Jaeger by excising a small piece of skin in which the tick's head was firmly embedded. On May 21 the patient had a hard chill with a subsequent fever and headache. These symptoms became more severe and the patient was sent to the hospital the following morning. On admission the patient was well nourished and well developed and had a distinct dusk flushing of the face; he complained of a severe backache, headache and aching of the bones and joints. He appeared acutely ill; there were no abnormalities in the chest or abdomen except the injury of the abdominal wall at the point at which the tick had been removed. The temperature was 100.6 F. A provisional diagnosis of a tick-borne infection was made. On May 23 the flexor surfaces began to break out with a light red distinct macular cutaneous eruption which disappeared on pressure. During the next four days the eruption continued to spread until it involved the entire cutaneous surface, being sparse over the face. The individual macular lesions enlarged and in many areas coalesced, forming bizarre shaped plaques. The entire eruption became dark red and no longer would fade on pressure, since it had now become very definite hemorrhagic spots. The appearance of the eruption changed very little during the next two weeks. During the first three weeks after admission the patient had a stormy course, being seriously ill, the temperature ranging between 101 and 104 F. and the pulse rate between 100 and 120. He was semicomatose but could be aroused, and when aroused he appeared quite clear mentally. On the twenty-first day the temperature dropped to normal and remained at that level. He left the hospital on the twenty-ninth day with pigmentation of the skin remaining at the points of the eruption and with definite evidence of myocardial damage. The white blood cell count remained between 12,000 and 20,600 during the period of hospitalization and the Weil-Felix reaction was positive on June 10.

CASE 3.—A white man aged 62, a carpenter, was admitted to the Colorado General Hospital May 19, 1937 at 5:30 p. m. He had for the last twelve months been making rustic tables for the tourist camp at Lyons, Colo. For some days he had been working in the timber getting wood for these tables. On May 9 he had chills. The next day he tried but was unable to work as vomiting began and he could not hold anything on his stomach. On Wednesday, the third day, he was taken to his home. At this time there were some red spots on his arms and chest. After he came home his chills and fever continued and his temperature was once recorded at 105 F. During the last few days his rash increased. He had become very apathetic and confused mentally. The patient had a florid complexion, his eyes were rather badly inflamed and he breathed noisily through his mouth. He appeared extremely toxic. The physical examination was not remarkable and nothing of any great significance was encountered with the exception of the rash which covered the entire body surface except the face. The rash was maculopapular and did not fade on pressure. It appeared to represent small hemorrhages in the cutaneous capillaries. The chest was examined carefully because the

breathing was peculiar; there seemed to be no particular explanation for the apparently labored breathing. The chest was resonant and no rales or adventitious breath sounds were elicited. The urine was practically normal. The white blood cell count showed 14,680 leukocytes with a differential of 94 per cent polymorphonuclears. The temperature on admission by rectum was only 102 F. and a few hours later dropped to 100.4 F. by rectum. The pulse, however, crossed the temperature curve and rose to 120. The patient was confused mentally. May 21 at about 5:15 or 5:20 p. m. he became very much confused and began breathing strenuously. The breathing was not the short, gasping of true dyspnea but seemed to be a breathing produced by an unusual respiratory stimulation. The breaths were full and the expansions of the chest were full, but the number of respirations were 45 or 50 a minute. At this time there was nothing on auscultation of the chest to indicate any respiratory or cardiac difficulty within the chest itself. The patient at first aroused when spoken to and turned his eyes in the direction of the speaker, but he was unable to speak. The respirations soon slowed and then ceased, the heart continuing to beat for several minutes. The patient was pronounced dead at 6:20, just about an hour after the onset of the rapid respiration and the coma. Permission for autopsy was obtained and the diagnosis of Rocky Mountain spotted fever was confirmed by the department of pathology by guinea pig inoculation of postmortem heart's blood and by microscopic examination of the cutaneous and visceral lesions.

SUMMARY

1. The literature shows that cases of Rocky Mountain spotted fever have been reported from thirty-seven of the forty-eight states.

2. Rocky Mountain spotted fever is transmitted to human beings through infected ticks, and the causative organism is Dermacentroxenus rickettsii.

3. Three types of the disease are recognized: the mild, the severe and the fulminating.

4. The cutaneous manifestations of Rocky Mountain spotted fever are characteristic.

5. A drug exerting any great amount of specific action against this infection has not been found.

6. Vaccine gives partial protection for a period of one year or less.

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ABSTRACT OF DISCUSSION

DR. RICHARD J. BAILEY, Spokane, Wash.: I congratulate Dr. Hutton on his comprehensive summary of our knowledge of this disease. It is important to emphasize that the term "Rocky Mountain spotted fever" is a misnomer. The disease is not localized in the Rocky Mountain states or even in the Bitter Root Valley but is found, roughly, throughout the entire country, as it has been reported in all the states except Wisconsin, Michigan and four New England states. It is important also to reemphasize that there is no distinction between the eastern and the western type of this disease. Tourists rarely acquire the disease because they are more alert to the menace when they are in tick infested areas. There is one good reason for a dermatologist to discuss a disease which is primarily in the realm of general medicine. This reason may be expressed in an objection to the use of the term "characteristic eruption" in Rocky Mountain spotted fever, because we all know that we have seen exactly similar pictures in subacute disseminated lupus erythematosus, in severe toxic types of drug eruptions and in many other conditions. According to Dr. Parker, director of the Spotted Fever Institute, the differential diagnosis of this disease is becoming more difficult because the eruption has been modified by vaccination and because of the widespread use of the sulfanilamide type of drug. In these days such drugs are given early in any undiagnosed febrile disease, and we are often confronted with a mixed or a definite drug eruption in addition to the disease itself. Dr. Parker stated recently that one fourth of the vaccine available this year has been prepared from chick embryo and that next year one half of the quantity distributed will be of that type. It has been in use, however, for too short a time to evaluate it and predict any superiority to the type available at the present time. I should like to ask Dr. Hutton for any information that he may have regarding the new therapeutic vaccine for this disease, publicized recently in lay magazines.

THE EFFECT OF RENIN ON EXPERIMENTAL RENAL HYPERTENSION IN THE DOG

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AND
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Of the numerous methods reportedly available for producing hypertension in animals [1] (table 1), the most satisfactory is that of constriction of the renal arteries reported by Goldblatt [2] in his now classic experiment. During the past several years, moreover, there has accumulated growing evidence of similarity between experimental renal (Goldblatt) hypertension in the dog and essential hypertension as found in the great majority of patients so diagnosed [3] (table 2). Although a therapeutic agent which is effective in experimental renal hypertension may prove ineffective in essential hypertension, and vice versa, any new therapy proposed for essential hypertension should first receive an adequate trial in experimental renal hypertension. As a consequence, a number of attempts have been made to reduce the blood pressures of renal hypertensive dogs. Only a few of these efforts have met with some degree of success.

Thus Davis and Barker [4] reported that potassium thiocyanate reduced the blood pressures of dogs with renal hypertension. Both Weeks and his associates [5] and Cerqua and Samaan [6] found that nephrosplenopexy caused a more or less permanent decrease in the blood pressures of dogs rendered hypertensive by the Goldblatt technic. Katz and his co-workers [7] reported that transplanted autolyzing kidney tissue reduced the blood pressures of dogs with renal hypertension, but Goldblatt [8] could not confirm their finding. Harrison and his collaborators [9] reported reductions in the blood pressures of dogs with renal hypertension and of human

Messrs. Bernard Gomberg and M. L. Goldberg assisted the authors in this work.

Technical assistance was furnished by the Work Projects Administration, Project 30278.

This work was aided by a grant from the Graduate School Research Fund of the University of Illinois.

From the Departments of Physiology and Physiological Chemistry, University of Illinois College of Medicine.

Read before the Section on Pathology and Physiology at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 6, 1941.

1. Blalock, Alfred: Experimental Hypertension, Physiol. Rev. **20:** 159 (April) 1940.

2. Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59:** 347 (March) 1934.

3. Goldblatt, Harry: Studies on Experimental Hypertension: XII. The Experimental Production and Pathogenesis of Hypertension Due to Renal Ischemia, Am. J. Clin. Path. **10:** 40 (Jan.) 1940. Blalock.[1]

4. Davis, Loyal, and Barker, M. H.: Clinical and Experimental Experiences in Surgical Treatment for Hypertension, Ann. Surg. **110:** 1016 (Dec.) 1939.

5. Weeks, D. M.; Steiner, Alfred; Mansfield, J. S., and Victor, Joseph: The Depressor Effect of Spleno-Reno-Pexy on Hypertension Due to Renal Ischemia, J. Exper. Med. **72:** 345 (Oct.) 1940.

6. Cerqua, S., and Samaan, Adli: Cure of Experimental Renal Hypertension, Clin. Sc. **4:** 113 (Dec.) 1939.

7. Rodbard, S.; Katz, L. N., and Sokolow, Maurice: Reduction of Arterial Hypertension by Subcutaneous Implantation of Kidney Tissue, Proc. Soc. Exper. Biol. & Med. **44:** 360 (June) 1940.

8. Goldblatt, Harry, in discussion on Roth, G. M.; Robinson, F. J., and Wilder, R. M.: Response of the Blood Pressure to the Cold Pressor Test in Addison's Disease During Treatment with Desoxycorticosterone Acetate, J. A. M. A. **116:** 2430 (May 24) 1941.

9. Grollman, Arthur; Williams, J. R., Jr., and Harrison, T. R.: Reduction of Elevated Blood Pressure by Administration of Renal Extracts, J. A. M. A. **115:** 1169 (Oct. 5) 1940.

beings with essential and malignant hypertension by means of a kidney extract containing the antipressor substance believed to be present in normal kidney tissue. Because of untoward effects observed in a number of their dogs, as well as for other reasons, these authors reserved judgment relative to the ultimate specificity and value of this form of therapy. Page and his associates,[10] using a similar antipressor kidney extract, likewise reported favorable effects on the blood pressures of hypertensive dogs and human beings. Both of these groups considered this antipressor substance to be different from any of the known depressor agents.

In spite of these advances, however, the treatment of experimental renal hypertension in the dog and essential hypertension in man is still an unsettled problem. Obviously the production of an increase in collateral circulation to the constricted kidney by nephrosplenopexy has at best a limited applicability to the therapy of essential and malignant hypertension in man, since, if renal ischemia is involved in the pathogenesis of the clinical condition, it is ordinarily because of arteriolosclerosis rather than narrowing of the renal arteries. More work is necessary to determine the comparative effectiveness of the type of kidney extract used by Harrison and by Page and other known anti-

TABLE 1.—*Methods of Producing Experimental Hypertension*

1.	Desoxycorticosterone
2.	Continuous intravenous infusion of epinephrine
3.	Hypervitaminosis D
4.	Intracisternal injection of kaolin
5.	Bilateral section of carotid sinus and aortic depressor nerves
6.	Kidney antiserum nephritis
7.	High voltage irradiation of kidneys
8.	Ureteral obstruction
9.	Partial obstruction of renal veins
10.	Cellophane perinephritis
11.	Constriction of renal arteries

hypertensive agents, as well as its specificity for experimental renal hypertension and clinical essential or malignant hypertension.

A year ago we[11] reported the successful production of an antiserum for dog renin in the rabbit and for hog renin in the dog. The active principle of the antiserums, which we designated "antirenin," was shown to neutralize the acute pressor effect of the antigenic renin (illustrated in the tracing). Since then we have produced antiserums for various species of renin in different species of animals, as shown by table 3. As indicated by this table, moreover, dog renin in the dog and rabbit renin in the rabbit failed to produce an antiserum for renin, thus demonstrating that the production of antirenin depends on the heterologous character of the injected renin. The antiserums were also shown to neutralize not only the acute pressor effect of the antigenic renin but also that of other species of renin. Thus, for example, dog antiserum against hog renin neutralized the acute pressor effect of dog renin.

In view of these observations relative to antirenin and of the increasing possibility that renin is the pathogenetic pressor agent released from the constricted kidney in experimental renal hypertension, we studied the effect of hog renin on the blood pressures of dogs with renal hypertension. Our original thesis, of course, was that if renin was the pathogenetic pressor agent in experimental renal hypertension, the injection of heter-

TABLE 2.—*Similarities Between Experimental Renal Hypertension and Essential Hypertension*

1.	Reduced (?) renal blood flow
2.	Essentially normal renal function tests
3.	Normal cardiac output, blood volume, blood viscosity, and elasticity of arteries
4.	Increased peripheral resistance, chiefly arteriolar
5.	Normal pulmonary circulation pressures
6.	Normal blood chemistry
7.	Essentially normal hematologic picture
8.	Endocrines (adrenals, pituitary, gonads and thyroid) not involved pathogenetically
9.	Arteriolosclerosis involving various organs conditioned by duration hypertension
10.	Increased renin content of kidney

ologous hog renin into dogs with renal hypertension might lead to a reduction in blood pressure as the result of the in vivo neutralizing effect of antirenin so produced.

METHODS

Dogs were rendered hypertensive by the Goldblatt technic and the resulting hypertension was allowed to stabilize over a period of from three to twenty-three months before injections of renin were begun. Mean blood pressure readings were obtained by puncture of a femoral artery two or three times a week. Studies on the blood urea nitrogen, urinalyses and determinations of the body weight were made at biweekly intervals. The dogs were treated with daily intramuscular injections of renin for four months each. The renin solutions used were equivalent to 1 Gm. of fresh kidney cortex per cubic centimeter of solution and were administered in a dose of 1 cc. per kilogram of body weight. The method used for the preparation of renin was essentially that described by Grossman,[12] except that acetone was used as a dehydrating agent and much of the associated protein was removed by isoelectric precipitation. To date 4 dogs with hypertension have been treated with hog renin, 2 with hog renin inactivated

TABLE 3.—*Antiserums for Various Renins Produced in Different Species*

Renin of	Animal Injected	Result
Hog	Dog	Antirenin
	Rabbit	Antirenin
	Guinea pig	Antirenin
Dog	Rabbit	Antirenin
	Dog	No antirenin
Rabbit	Dog	Antirenin
	Guinea pig	Antirenin
	Rabbit	No antirenin
Cat	Rabbit	Antirenin
	Guinea pig	Antirenin

by heating at 70 C. for one-half hour and 2 with (homologous) dog renin.

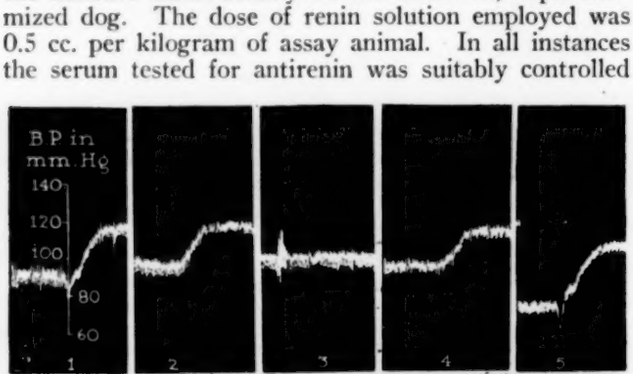
Blood serums were examined for antirenin before treatment and subsequently at two week intervals. The technic previously described[11] consisted essentially in mixing 2 volumes of serum with 1 volume of renin

10. Page, I. H.; Helmer, O. M.; Kohlstaedt, K. G.; Fouts, J. P., and Kempf, G. F.: Reduction of Arterial Blood Pressure of Hypertensive Patients and Animals with Extracts of Kidneys, J. Exper. Med. **73**: 7 (Jan.) 1941.

11. Johnson, C. A., and Wakerlin, G. E.: Antiserum for Renin, Proc. Soc. Exper. Biol. & Med. **44**: 227 (May) 1940.

12. Grossman, E. B.: Preparation of Extracts of the Renal Pressor Substance, Proc. Soc. Exper. Biol & Med. **39**: 40 (Oct.) 1938.

solution, allowing the mixture to stand at least overnight at 4 C. and assaying the acute pressor effect of the mixture intravenously on the etherized, nephrectomized dog. The dose of renin solution employed was 0.5 cc. per kilogram of assay animal. In all instances the serum tested for antirenin was suitably controlled



Section 3 shows neutralization effect of (rabbit) antiserum on pressor response to dog renin. Sections 2 and 4 are controls in which normal rabbit serum and dog renin were used. Sections 1 and 5 show pressor response to dog renin alone.

with serum from normotensive dogs and frequently with serum from untreated hypertensive dogs. Antirenin titers for both hog and dog renins were determined.

At the present writing, 1 of the 4 dogs which received hog renin has been observed for twelve months and the other 3 have been observed for eight months since treatment has been discontinued. The 2 dogs given inactivated hog renin and the 2 animals injected with dog renin have been under observation for four months and two months respectively since the cessation of treatment.

When the results in these 8 animals became apparent, we decided to reverse our experiment and also study the effect of renin similarly administered to normotensive dogs prior to constriction of the renal arteries. Accordingly, 2 normotensive dogs were observed during a control period of three months. Hog renin was then injected for approximately six months; in the middle of this period the renal arteries were constricted three weeks apart. Two months have elapsed since the injections with hog renin have been discontinued. Determinations of blood pressure, studies on

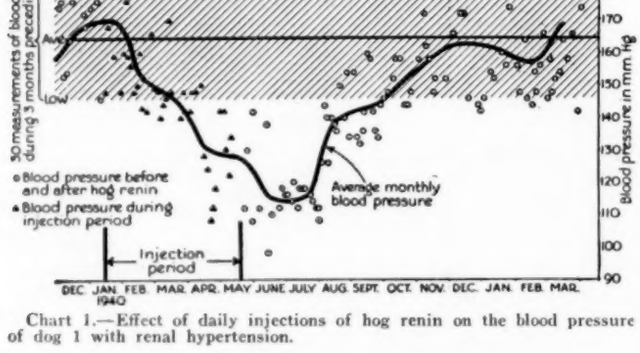

30 measurements of blood pressure during 3 months preceding renin
High
Ave.
Low
Blood pressure in mm Hg
Average monthly blood pressure
Blood pressure before and after hog renin
Blood pressure during injection period
Injection period
DEC. JAN. FEB. MAR. APR. MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MAR.
1940

Chart 1.—Effect of daily injections of hog renin on the blood pressure of dog 1 with renal hypertension.

the blood urea nitrogen, urinalyses, determinations of body weight and assays of antirenin were likewise made on these 2 animals.

RESULTS

Hog Renin in Hypertensive Dogs.—The intramuscular injections of hog renin produced striking reductions in the blood pressures of the 4 hypertensive dogs. These results are presented graphically in charts 1 to 4.

The first hypertensive dog showed an average femoral blood pressure of 164 mm. of mercury with a maximum of 184 mm. and a minimum of 146 mm. during the three months preceding treatment. As shown by chart 1, the blood pressure of the animal fell more or less steadily throughout the period of injections of hog renin until the normal or prehypertensive range was reached in the fourth month of treatment. During the two months following renin therapy, the blood pressure dropped somewhat below the original normotensive level. In the succeeding five months the pressure slowly rose to reach the pretreatment hypertensive range, at which it has remained for the past five months.

The second dog was hypertensive for nine months prior to the injections of renin, although only the last six

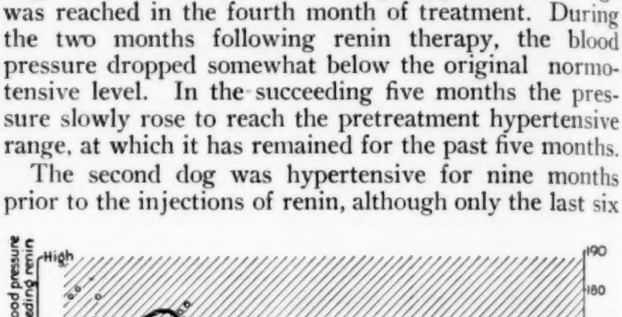

30 measurements of blood pressure during 6 months preceding renin
High
Ave.
Low
Blood pressure in mm Hg
Average monthly blood pressure
Blood pressure before and after hog renin
Blood pressure during injection period
Injection period
1940 MAR. APRIL MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MAR.

Chart 2.—Effect of daily injections of hog renin on the blood pressure of dog 2 with renal hypertension.

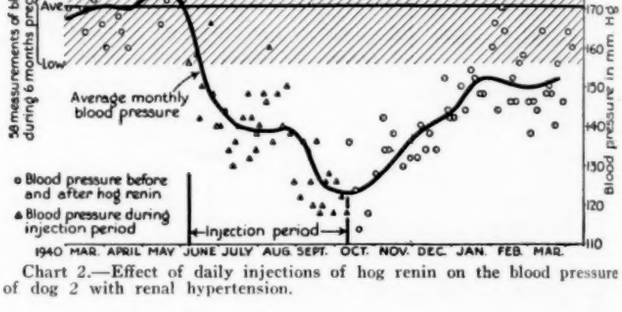

84 measurements of blood pressure during 8 months preceding renin
High
Ave.
Low
Blood pressure in mm Hg
Average monthly blood pressure
Blood pressure before and after hog renin
Blood pressure during injection period
Injection period
1940 MAR. APR. MAY JUNE JULY AUG. SEPT. OCT. NOV. DEC. JAN. FEB. MAR.

Chart 3.—Effect of daily injections of hog renin on the blood pressure of dog 3 with renal hypertension.

months of this period are recorded in chart 2. As illustrated, the blood pressure decreased during the four months of treatment until the prehypertensive level of the animal was reached by the end of the third month and a range slightly below the original normotensive level was attained in the fourth month. During the eight months following treatment the pressure has gradually risen to practically the pretreatment hypertensive level.

The third dog was hypertensive for seventeen months prior to renin therapy, although only the last eight months of this period are recorded (chart 3). As indicated, the blood pressure fell to the prehypertensive level by the end of the second month of treatment and remained in this range throughout the remainder of the treatment period. During the months that have elapsed since the last injection of renin, the blood pressure has shown a gradual rise to the hypertensive range.

The fourth dog (chart 4) was hypertensive for twenty-three months before injections of hog renin were begun, the last fifteen months of this period being recorded. The blood pressure of this dog fell to the lower limits of the hypertensive range during the first two months of treatment and remained there for the rest of the treatment period. During the two months following injections of renin, the pressures continued essentially unchanged but subsequent to this showed an abrupt return to the pretreatment hypertensive level, where they have remained.

At no time during treatment or subsequently was there any clinical evidence of untoward effects. The appetites of the 4 dogs remained excellent, their weights constant and their blood urea nitrogens and urines remained normal throughout the period of observation.

Before the administration of hog renin, the serums of the dogs showed no neutralizing effect (antirenin) for hog or dog renin. Repeated examinations of the serums of 40 normotensive and 10 untreated hypertensive dogs used as controls likewise showed no neutralizing effect for these renins. Antirenin to hog renin became demonstrable by the end of the first month of treatment and with variations in the 4 dogs reached a sufficient titer by the end of the third month to neutralize completely the acute pressor effect of hog

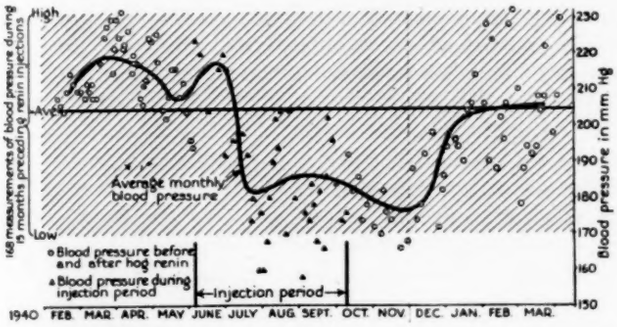


Chart 4.—Effect of daily injections of hog renin on the blood pressure of dog 4 with renal hypertension.

renin by the assay technic employed. With fluctuations, the antirenin titer for hog renin has remained essentially unaltered in the first dog up to the present time (some twelve months since treatment has been discontinued). In the other 3 animals, on the contrary, antirenin disappeared from the serums more or less coincidentally with the return of the blood pressures to the pretreatment hypertensive range. The neutralizing effects of the serums of the treated animals for dog renin closely paralleled the antirenin titers for hog renin.

Inactivated Hog Renin in Hypertensive Dogs.—The intramuscular injections of inactivated hog renin produced no significant change in the blood pressures of the 2 hypertensive dogs so treated. The results for 1 of the dogs are illustrated by chart 5.

This dog was hypertensive for seven months before injections of inactivated hog renin were begun, the last three and one-half months of this period only being recorded in chart 5. A slight but not significant rise in blood pressure occurred during the four month period of injections. In the four months since the discontinuance of injections there has been no significant change in the hypertensive level.

The results with the second dog were completely comparable. Not only did the inactivated hog renin have no effect on the blood pressures of the hypertensive dogs but antirenin failed to appear in the serums. Likewise, there were no toxic manifestations noted in either of the animals.

Dog Renin in Hypertensive Dogs.—The injections of dog renin into 2 hypertensive dogs resulted in a

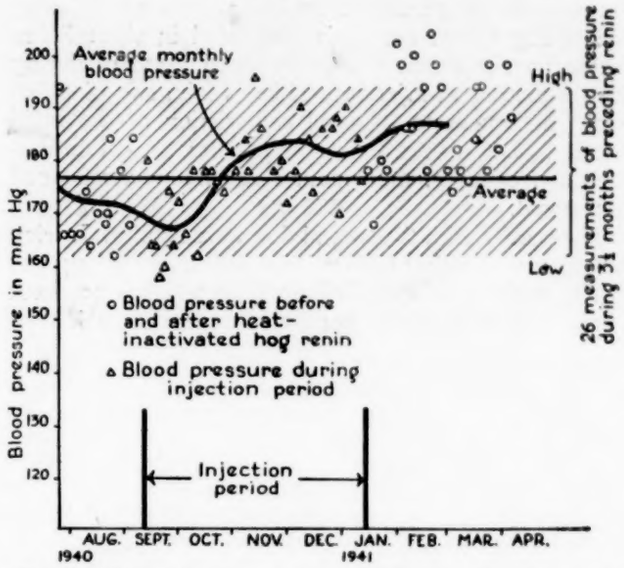


Chart 5.—Effect of daily injections of inactivated hog renin on the blood pressure of a dog with renal hypertension.

moderate but significant rise in blood pressure, as illustrated by chart 6.

The dog whose course is charted was hypertensive for three months preceding injections of dog renin. During the second month of injections there was a more or less abrupt rise of approximately 25 mm. of mercury in the average monthly blood pressure, which persisted throughout the period of injections and has remained

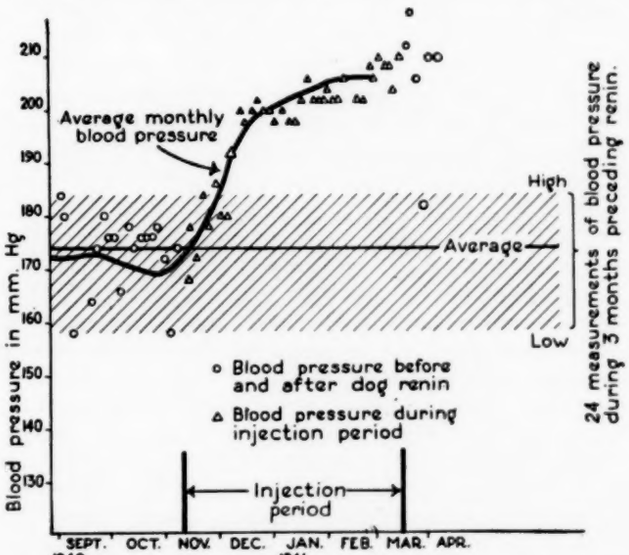


Chart 6.—Effect of daily injections of dog renin on the blood pressure of a dog with renal hypertension.

during the two months of observation since the injections have been discontinued.

Similar results were obtained with the second dog. Repeated assays for antirenin against both hog and dog renins gave uniformly negative results in both dogs. Neither animal showed any detectable evidence of toxic effects from the injections.

Hog Renin in Normotensive Dogs.—The intramuscular injections of hog renin produced no significant change in the blood pressures of the 2 normotensive dogs. Bilateral constriction of renal arteries likewise failed to produce any significant change in blood pressure, contrary to the customary hypertensive response in the untreated animal (chart 7).

The dog whose course is illustrated in chart 7 has shown no significant change in blood pressure during the six months of injections of hog renin, two of which were subsequent to bilateral constriction of the renal arteries. During the two months since the discontinuance of treatment, the pressure has likewise remained unchanged.

The results with the second dog were similar. During the second month of injections antirenin to hog and to dog renin developed in both dogs and has persisted to date. The 2 animals appear otherwise normal.

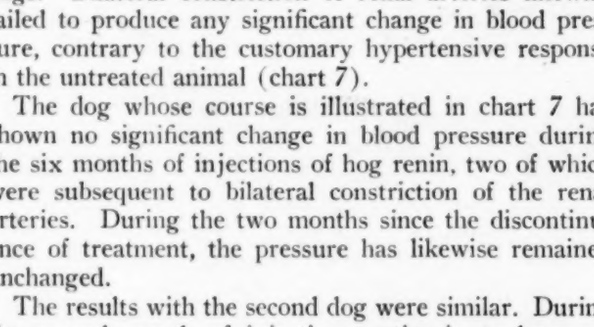


Chart 7.—Effect of daily injections of hog renin on the blood pressure of a normotensive dog before, during and after constriction of renal arteries.

COMMENT

This report is obviously preliminary in character. However, the blood pressure reductions obtained in the 4 hypertensive dogs by treatment with hog renin, in the absence of any overt evidence of toxic effects, are so striking that we have good reason to believe that they will be duplicated on a larger group of animals. In general there was some correspondence between the magnitude of the fall in blood pressure and the length of the period of hypertension preceding treatment with hog renin. Thus, as indicated by charts 1 to 4, the decrease in blood pressure was greatest in the first dog, which had been hypertensive for only three months, and least in the fourth animal, which had been hypertensive for nearly two years preceding injections of hog renin. Most probably these differences are related to the degree of arteriolosclerotic change present. We likewise expect to duplicate the negative results with inactivated hog renin and with dog renin in larger groups of dogs with renal hypertension.

In addition to the controls with heat-inactivated hog renin and with dog renin, other control experiments are necessary: 1. The effect of other species of renin must be studied. At the present time we are conducting experiments with rabbit renin in experimental renal hypertension. We predict that while the homologous (dog) renin will not lower the blood pressure of a renal hypertensive dog, any heterologous renin most probably will. 2. The effect of highly purified preparations of renin as well as the optimal frequency, dosage and mode of administration must be studied. 3. The action of extracts of various tissues from the hog and other species prepared after the manner of renin must be determined.

We have already emphasized the lack of harmful effects in these dogs given injections of various renins. The absence of albuminuria is cogent evidence against significant renal damage.[13] However, in view of the toxic effects of kidney extracts in nephrectomized dogs reported by Winternitz and his associates,[14] we propose to examine our dogs with additional tests for renal, hepatic and other functions, as well as grossly and microscopically at necropsy. Worthy of note is the fact that, contrary to the suggestion of others,[15] the observed reduction in blood pressure per se did not cause toxic manifestations.

Certainly much work must be done before the mechanism of these striking reductions in the blood pressures of the 4 hypertensive dogs produced by hog renin is clarified. The fact that the hog and dog antirenin titers of the serums of the 4 animals rose simultaneously with the reductions in blood pressure and likewise fell more or less coincidentally with the return of the blood pressures of 3 of the 4 animals to the hypertensive range suggests the possibility that antirenin may be responsible. However, as previously stated, antirenin has persisted in the serum of the first dog treated with hog renin in spite of the fact that the blood pressure of the animal has been in the pretreatment hypertensive range for the past five months. This obviously speaks against the antirenin hypothesis. On the other hand, inactivated hog renin and active dog renin both failed to reduce the blood pressures of dogs with renal hypertension and likewise did not lead to the production of antirenin. The observation that the acute pressor effect of intravenously administered hog and dog renins was obtained in our treated hypertensive and normotensive dogs in the presence of antirenin should likewise not be construed against the antirenin hypothesis, since we have found that the in vitro neutralization of renin requires a period of hours. Of possible significance also is our finding that the typical renin curve is modified in the animals showing antirenin in that the blood pressure return is more rapid than normal. The fact that a heterologous (hog) renin and not the homologous (dog) renin was effective speaks for the probability that the reductions in blood pressure of the 4 hypertensive dogs resulted from some type of immune or antihormone response to renin or less probably to some other heat labile constituent of the kidney cortex of the hog. Another, though less likely, possibility is the presence of a significantly greater concentration of some directly antihypertensive agent in the hog renin solution as compared with the dog renin solution.

The group of 2 dogs prophylactically treated with hog renin and thereby protected against the hyperten-

13. Brucer, Marshall, and Robinson, S. C.: Hypertension and Kidney Function: Relationship of Albuminuria to Blood Pressure, Weight, Body Build and Surface Area, Am. J. Clin. Path. **10:** 800 (Nov.) 1940.

14. Winternitz, M. C.; Mylon, E.; Waters, L. L., and Katzenstein, R.: Studies on Relation of Kidney to Cardiovascular Disease, Yale J. Biol. & Med. **12:** 623 (July) 1940.

15. Williams, J. R., Jr.; Grollman, Arthur, and Harrison, T. R.: The Reduction of the Blood Pressure of Hypertensive Dogs by the Administration of Renal Extract, Am. J. Physiol. **130:** 496 (Sept.) 1940.

sive effect of bilateral renal artery constriction is admittedly small and must be increased before final conclusions can be drawn. Moreover, suitable control experiments must be performed. The absence of hypertension in these 2 animals, however, is most probably not fortuitous, since we have never failed to obtain some degree of hypertension in more than 50 dogs subjected to bilateral constriction of the renal arteries by a similar technic. We have been watching these 2 dogs with considerable interest since hog renin therapy was stopped two months ago. If the antirenin titers of the animals fall as their blood pressures rise to a hypertensive level during the next several months, the antirenin hypothesis will be strengthened but by no means proved.

Without much question the antihypertensive action of the injections of hog renin was not due to the coincidental presence of the antipressor substance under investigation by Harrison and his co-workers [9] and by Page and his associates.[10] Thus the amounts of kidney equivalent used by them were much larger than those employed by us, the blood pressure reductions produced by therapy were more prompt in their animals than in ours and the blood pressure increases following the cessation of treatment usually occurred earlier in their dogs than in ours. Furthermore, no signs of toxicity accompanied the reductions in blood pressure in our dogs. Moreover, Harrison and his associates [16] have shown that their principle inhibits the acute pressor effect of renin and that it is extractable from dog kidney and, presumably when so obtained, effective in the hypertensive dog. On the other hand, Page and his associates [10] state that their antipressor extracts contain renin.

If the promise of our preliminary observations is substantiated by further work in the experimental animal, this type of treatment will be studied in essential hypertension in man.

CONCLUSIONS

1. Daily intramuscular injections of hog renin for four months produced striking reductions in the blood pressures of dogs with renal hypertension, whereas heat-inactivated hog renin and active dog renin were without effect.

2. No detected toxic manifestations resulted from the injections of renin or from the reductions in blood pressures.

3. The serums of the dogs treated with hog renin, but not the serums of the dogs given injections of inactivated hog renin or dog renin, neutralized the acute pressor effect of renin (antirenin).

4. Daily intramuscular injections of hog renin into 2 normotensive dogs before and after constriction of the renal arteries prevented the development of hypertension.

5. The mechanism of these therapeutic and prophylactic effects of hog renin in experimental renal hypertension in the dog is not clear. Most probably an immune (antihormone?) response to heterologous hog renin is involved.

1853 West Polk Street.

16. Grollman, Arthur; Williams, J. R., Jr., and Harrison, T. R.: Preparation of Renal Extracts Capable of Reducing Blood Pressure of Animals with Experimental Renal Hypertension, J. Biol. Chem. **134:** 115 (June) 1940.

ABSTRACT OF DISCUSSION

DR. HARRY GOLDBLATT, Cleveland: The treatment of renal disease, with or without hypertension, in man, especially so-called essential hypertension, by the administration of renal substances in various forms and by various methods, is very old. The directing idea of this form of therapy was always substitution for some form of deficiency, hormonal or otherwise. The treatment of hypertension, experimental or otherwise, by the injection of a pressor substance, with the idea of developing an antipressor substance in the blood, is immunologically old but for this particular problem quite new. I am sure, from what Dr. Wakerlin has said, that he and Dr. Johnson are aware of the danger of concluding that the effects they observed in these few incomplete experiments were actually due to the development of an antipressor substance in the blood. They have pointed out that in the first dog, their best experiment, after the cessation of therapy, the blood pressure promptly returned to the original high level, although the antipressor substance, the antirenin, remained at the original high level. This inconsistency remains unexplained and many more experiments must be performed to elucidate this point. Other investigators have succeeded in reducing the blood pressure in hypertensive animals and man by means of renal extracts that are supposed to contain antipressor or so-called inhibitor substance. Dr. Lewis, Dr. Kahn and I have found that these extracts, which are supposed to contain only antipressor or inhibitor substances, also contain renin in much greater concentration than in the extract which was used by Drs. Wakerlin and Johnson. It is at least possible, therefore, that the effects which are being attributed to antipressor or inhibitor substances in the extracts used by these other investigators are due, after all, to renin. It is equally true that Drs. Wakerlin and Johnson are dealing with very crude products and not with pure renin, so that the effects which they have obtained may possibly be due either to inhibitor or to antipressor substance present in their extract. All investigators should refer to the products they are using merely as renal extracts, identified by letter or number, and not as renin, or inhibitor or by any other name, until the effective substance, in pure form, is isolated and identified. All the investigators are dealing with relatively crude products. It would be well, therefore, to refrain from any controversy about whether the effective substance is renin or inhibitor. Neither has yet been proved. It should, however, be the common endeavor of all investigators in this field to isolate and identify the effective substance.

DR. LOUIS N. KATZ, Chicago: Dr. Myron Prinzmetal has informed me that he has been able to confirm the blood pressure lowering effect of hog renin on seven rabbits, using a technic similar to that of Wakerlin and Johnson. However, he found that an immediate rise in blood pressure occurred on injection during the period of lowered blood pressure and afterward, as well as in the control period. This would tend to oppose the idea that the pressure drop is due to an antihormone developing in the dog following the hog renin injections. I should like Dr. Wakerlin to comment on the results of Dr. Hessel, who a few years ago reported that injection of heterologous renin extracts in rabbits gives rise to a hypertension which persisted long after the injections were discontinued. I agree with Dr. Goldblatt that we must not be misled in our thinking by ascribing particular specific properties to these crude preparations, which probably contain many substances most of which are still unknown pressor or depressor materials. Early in our work we were impressed with the importance of the normal kidney as a mechanism for preventing or neutralizing renal hypertension. Dr. Rodbard and I found that the normal kidney far exceeded any other tissue in this ability, and this mechanism appears to be due to the metabolic activity of the normal kidney. We have done other experiments in which kidney tissue was implanted subcutaneously in hypertensive dogs and found that as we produced abscesses the blood pressure dropped toward normal and the drop persisted for some time after the abscesses had resolved. We carried out some one hundred and twenty-

five experiments including controls, of which twenty-five dealt with kidney implantation in hypertensive animals, and in all but three of the latter we obtained a similar depressor effect. In repeating this work Goldblatt found that implantation of kidney tissue had no effect on the blood pressure if no abscess was produced. This would apparently confirm our view that an abscess must be formed before the blood pressure lowering effect appears. However, this effect is apparently not dependent on infection, since, as Wakerlin showed, severe mixed infections do not affect the blood pressure, nor, as we found, does this occur with other than kidney abscesses. How these implant experiments are related to the extracts discussed today remains to be determined. While renal hypertension in the animal is apparently the only method so far available of reproducing a condition similar to essential hypertension in man, it is not true that clinical essential hypertension is necessarily renal in its origin. While the kidney may be the intermediate step in its production, the renal changes are produced by some other factor.

DR. JOHN R. WILLIAMS, Winston-Salem, N. C.: My associates and I have recently attempted to confirm this interesting work of Wakerlin and Johnson. We treated 2 dogs with renin for two months with no drop in blood pressure. Several reasons may account for our inability to confirm their results; the period of treatment was rather short. Renin is not a pure substance but a crude extract and when prepared in different ways has different pharmacologic properties, so that it seems possible that renin prepared one way might give this effect. Whether the effects observed by Wakerlin and Johnson are the same as those induced by the renal antipressor substance cannot be decided without further work.

DR. G. E. WAKERLIN, Chicago: It is obvious, as Dr. Goldblatt said, that we must have more experiments. Possibly we are dealing with the antipressor substance which Harrison and Page have reported on, but this is unlikely. It is possible also that Harrison and Page have been working with the same mechanism which we are interested in. Certainly our extracts are crude. They contain not only renin but a number of substances of unknown character. If some directly antipressor substance is present in them, it must be present in appreciably greater concentration in hog renin than in dog renin. The fact that Dr. Prinzmetal was able to obtain a rise in blood pressure by the intravenous injection of renin into those rabbits is not against the antirenin hypothesis. As we pointed out, the mixing of the antiserum with renin requires a period of hours for complete neutralization. It is not surprising, therefore, that an acute intravenous injection of renin produces a pressor effect in animals showing antirenin. However, the pressor effect is not entirely typical, according to our findings, in that the return of the blood pressure is much more rapid than in the untreated hypertensive or normal animal. It is possible, therefore, for antirenin to neutralize a continuous release of small quantities of renin from the constricted kidneys of the Goldblatt dog. However, we emphasize again that we are not certain of antirenin being the mechanism. We too have found that repeated injections of renin, provided they are homologous, give rise not to a fall in blood pressure but to an increase. I do not recall Dr. Hessel's experiments well enough to remember whether he used heterologous or homologous renin. I agree with Dr. Katz that we cannot say that experimental renal hypertension in the animal is the same as essential hypertension in man. However, I do not think that any one is justified in using a proposed therapeutic agent in essential hypertension in man today without having previously tried it in experimental renal hypertension in the dog. We are interested in Dr. Williams' report that he has tested hog renin in two dogs by the same technic used by us, except that he injected the hog renin for only two months. I think he should have run his experiments as we did for at least four months. As he stated, he is drawing no conclusions. Dr. Williams emphasized the crude character of the renin solutions with which we have worked. We agree with all he said from that point of view.

THE SUPRASPINATUS SYNDROME

SYMPTOMATOLOGY, PATHOLOGY AND REPAIR

DAVID M. BOSWORTH, M.D.
NEW YORK

Since 1933 I have had 53 patients whose shoulders have been radically explored and repaired. In a previous communication the pathologic conditions found were reported, a classification offered and a new method of repair proposed.[1] I have made a follow-up examination of all except 3 patients. There have been no deaths, infections or major catastrophes.

There were 28 cases originally reported, and to these are added 25 others. My previous classification of the pathologic lesions found holds true for the new cases, but with the addition of two subheadings, namely 2 E and 4 C. The complete classification is as follows (fig. 1):

1. Pathologic condition not found, 2 cases.
2. Lesions of tendons.

A. Complete avulsion of the short rotator cuff (tendons of the supraspinatus, infraspinatus, teres minor and subscapularis muscles), 4 cases.

B. Laceration or avulsion of one or more short rotator tendons in their substance or at their attachments, 30 cases.

C. Musculotendinous separation of the supraspinatus and the infraspinatus muscles, 1 case.

D. Calcification or ossification of the supraspinatus tendon (plus surrounding calcification and degeneration), 5 cases.

E. Lesions of the subscapularis tendon (recurrent dislocation), 3 cases.

3. Bursal lesions.

A. Obliterative subacromial bursitis (frozen shoulder), 7 cases.

B. Laceration of the bursal floor without tendinous involvement, 1 case.

4. Lesions of bone.

A. Sharp exostosis at the tendinous attachment of the greater tuberosity without other pathologic condition, 1 case.

B. Rounded exostosis on the greater tuberosity associated with tendon laceration, 2 cases.

C. Osteochondritis.

(*a*) localized, 1 case.

(*b*) generalized, 1 case.

It must be noted that in certain instances double lesions existed and had to be classified under two headings. Hence the number of pathologic lesions found was in excess of the number of shoulders explored.

1. PATHOLOGIC CONDITION NOT FOUND

In my first series there was a patient aged 42 who had a classic picture of rupture of the supraspinatus tendon, with loss of abduction and an inconstant catch in the shoulder, localized tenderness and protection on unguarded motion. Operative intervention disclosed no pathologic condition whatever. A follow-up examination six and one-half years later revealed no defect in the shoulder except slight restriction of internal rotation. Another patient, a neurotic school girl aged 18, was found to be toying with the idea of a lawsuit. She

From the Orthopaedic Service at St. Luke's Hospital.
Read before the Section on Orthopedic Surgery at the Ninety-Second Annual Session of the American Medical Association, Cleveland, June 5, 1941.

1. Bosworth, D. M.: J. Bone & Joint Surg. **22**: 369-392 (April) 1940.

so readily assumed symptoms of deep surface tendon laceration that it was impossible to judge as to its actual presence or absence. On exploration considerable relaxation of the whole tendinous cuff seemed to be present, but no other pathologic condition was found. It is of course possible that the patient had a small osteochondritic defect in the humeral head underlying the supraspinatus or the infraspinatus tendon and that this defect, not having been previously recognized, was not found. (See class 4 C, *a*.) At a follow-up examination two years postoperatively complete recovery was observed.

to rule out damage to short rotator tendons, can scarcely be overemphasized. Operative repair of massive tendinous defects such as these, especially if associated with damage to the axillary nerve, has proved useless in my hands, and I would still advise arthrodesis as a primary procedure when such conditions are found.

B. *Laceration or Avulsion of One or More Short Rotator Tendons in Their Substance or at Their Attachments.*—I now have 30 cases of this condition. They are classified as follows:

1. Recent avulsion.

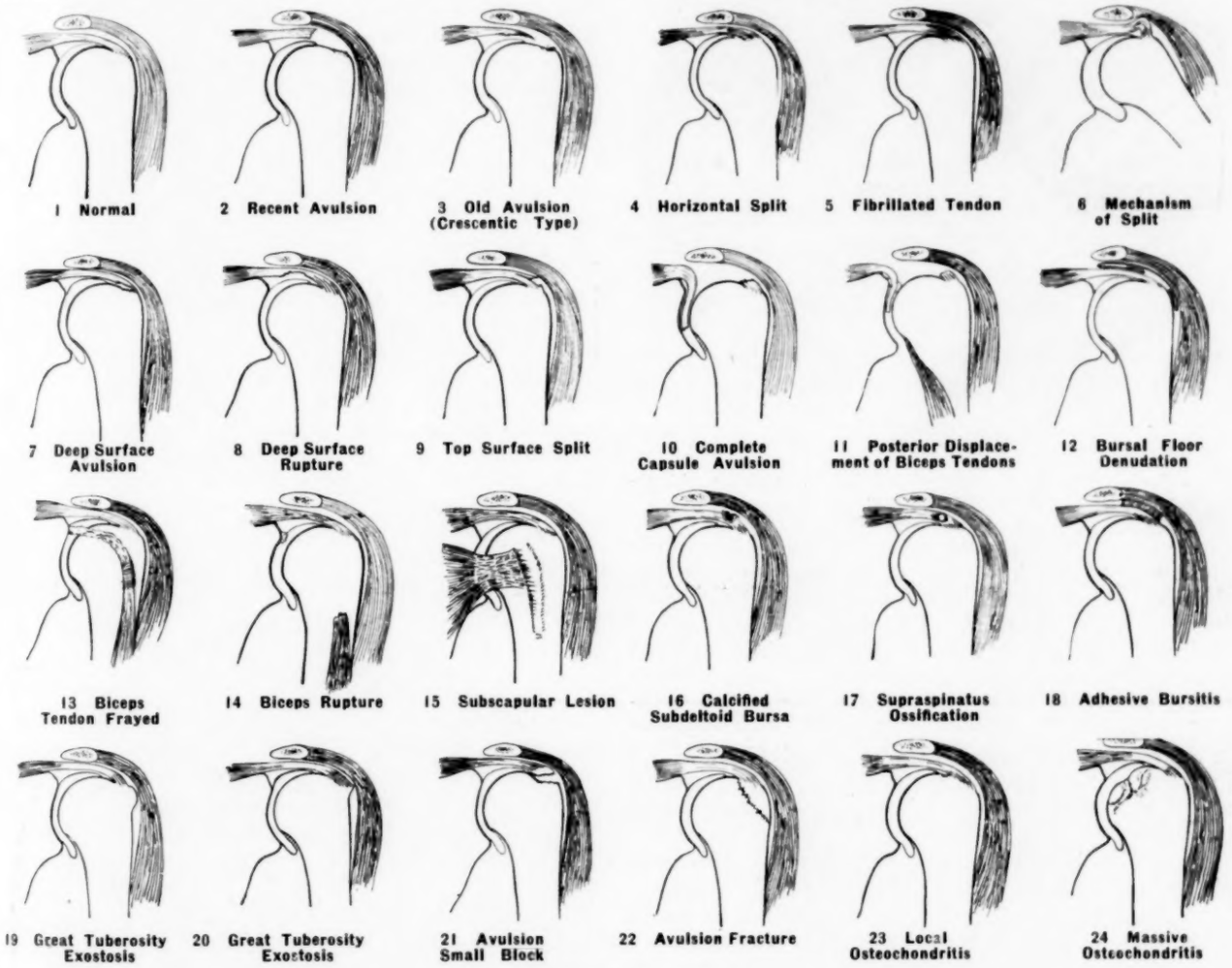


Fig. 1.—Types of lesion found.

2. LESIONS OF TENDONS

A. *Complete Avulsion of the Short Rotator Cuff.*—There have been only the original 4 patients with complete avulsion of the cuff. The treatment of 3 has been a complete failure, and the fourth, on whom an arthrodesis was done at the original operation, was the only one able to return to a gainful occupation. The typical picture of inability to maintain reduction after dislocation, the head merely being replaced over a tendinous cuff drawn downward across the glenoid cavity, was present. I have noted that 2 patients, both elderly, avulsed the cuff by simple falls on the outstretched arm, but that in 2 others the cuff was completely lacerated by forcible manipulation and reduction of simple dislocation without anesthesia. The importance of securing relaxation and using gentleness in the reduction of dislocation of the shoulder, with subsequent observation

(*a*) Of deep or superficial surface at insertion, 10 cases.

(*b*) Of entire thickness of tendons.

(1) Of anterior portion of supraspinatus tendon, 5 cases.

(2) Complete, of tendon or tendons, 8 cases.

(*c*) With horizontal split, 3 cases.

(*d*) With fibrillation or fimbriation, 1 case.

(*e*) Of cortical fragment at supraspinatus insertion, 1 case.

2. Old avulsion (crescentic type), 2 cases.

These lesions have occurred at any age from 17 to 70. The greater number are in men, there having been 21 in men in my series, as compared with 9 in women. In 18 cases the right shoulder was involved, and in 12, the left. Arthritic manifestations were not causative factors in any case. Injury was the universal etiologic

factor—a fall on the outstretched arm, a twist or an unusual lifting strain; in only 1 instance was there reported direct trauma to the shoulder with the arm at the side.

Two patients had both shoulders involved. One of these, previously reported, had accidental hyperextension of both shoulders under anesthesia in my presence. Successful repair of the lesion of the left shoulder was done, and symptoms rapidly disappeared from the right shoulder. The other patient had had trichinosis some years previously and had suffered twisting injuries to each shoulder of an amount which would ordinarily not be expected to result in rotator tendon laceration. Preceding dislocation had occurred in 3 patients: in 1 twelve years previously, in a second four times in the preceding three years and in a third at the time of the original injury, one month before operation.

Fig. 2.—Laceration of the supraspinatus tendon. Compare with the lesion, in another patient, shown in figure 3.

Symptoms have not consistently denoted the extent of the lesion. Pain, spasm and protection have always been present in some degree. They were more apt to occur with a partial laceration than with complete tears with retraction of the tendons. With the latter, massive loss of power and the so-called arm drop sign were more apt to predominate. The presence of a sulcus or an eminence was an extremely unreliable diagnostic sign. In the only instance in which this could be demonstrated, and in fact was photographed cinematographically, there proved not to be a tendon tear at all. Loss of active motion in all directions depended on spasm and protection from partial tears and on loss of power from complete ones. The range of passive motion was usually complete after complete tears but was limited by pain, spasm and protection after incomplete tears. Bursal adhesions were found frequently after incomplete tears but rarely after complete ones. This is so because after complete tears the bursal floor is retracted by the lacerated tendons and adhesions cannot form. Restriction of abduction of the arm on stooping was frequently associated with incomplete tears but not with complete ones. Atrophy frequently was difficult to demonstrate because of overlying adipose tissue and other musculature. When demonstrated it was generally associated with massive bursal adhesions, partial tears or the so-called rim rent tears.

The typical picture of a complete laceration of the supraspinatus tendon with or without laceration of other tendons closely paralleled the picture of complete avulsion of the cuff except for the fact that there was no recurrent dislocation. The patient lost all active power of abduction beyond the point at which the greater tuberosity of the humerus impinged against the acromial process, but passive abduction and other motion were complete and practically painless when the head of the humerus was manipulated downward so that impingement did not occur. Localized tenderness, a sulcus, an eminence and demonstrable atrophy might be absent. The arm drop sign, however, was strongly positive.

If one contrasts with complete lacerations the partial laceration, horizontal split, tear of the deep surface and all crescentic types of laceration, one sees an entirely different picture. The patient has considerable spasm and protection, with pain on active or passive motion. There is localized tenderness, often exquisite, but because of protection there is no catch in abduction and there is entire refusal to support the arm; hence there is no arm drop sign.

Definite, specific diagnosis of the lesion to be found cannot always be made preoperatively. The term "internal derangement" should be as applicable to the shoulder as it has become to the knee. From careful study, however, one may be reasonably sure that there are internal pathologic conditions although one cannot with certainty state the minute nature thereof.

From my present follow-up study of the outcome of repair I would again emphasize that after the initial injury to a shoulder in which laceration of the rotator tendon is suspected no harm can accrue from a delay in operation of a week or two for observation, to determine whether actual laceration or merely moderate stretching of tissues has been sustained. Throughout the second half of this series such delay has been undertaken in several instances, with the avoidance of

Fig. 3.—Laceration of the supraspinatus tendon with degenerative changes. Once the tendon is torn, lesions of this type do not heal.

operative repair in a few. I will grant that in some of the latter there may have been minor laceration, but I feel that the speed of recovery without operation justified conservative treatment. If the lesion is suspected, its diagnosis will soon be confirmed and repair can be instituted. When gross symptoms persist beyond

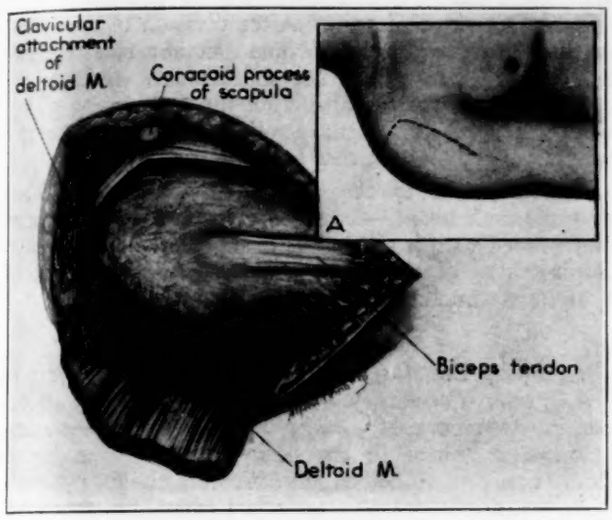


Fig. 4.—Operative repair: turning back the deltoid muscle from its acromial attachment.

two weeks after injury, suggesting major involvement of a short rotator tendon, repair should not be withheld. It has been definitely shown that the supraspinatus and infraspinatus tendons show only further degenerative changes as time progresses after laceration and that repair does not take place under conservative measures (figs. 2 and 3). When recovery takes place after minor tears it does so with wearing and smoothing of torn surfaces, accompanied by permanent degenerative changes.

I would again emphasize that at operation the superficial surface of the tendon may appear normal with a massive avulsion lesion of the deep surface. Exploration should not stop with the bursa but should include the deep surface of the tendon. This can be done through a small incision anterior to the supraspinatus tendon and the passage of a small curved clamp beneath it. If this procedure is carried out, horizontal splits within the tendon substance will likewise not be missed.

Of the 30 patients whose pathologic condition has been presented, 5 were operated on this year, and the results of course are unknown. The progress of the remaining 25 has been followed to the present time, the longest follow-up study lasting eight years and the shortest one year. Nine had perfect range of motion, normal strength, a lack of pain and an absence of symptoms. Two had slight pain but stated that it was present only in bad weather. Two had a slight loss of strength, although both are carrying on at a laborious occupation. Eight had slight restriction of motion amounting to as much as 10 per cent of abduction or rotation. The treatment of 4 has been classified as a failure. One of the 4 had subscapular bursitis, with an end result of gross crepitation on any motion of the scapula. A second relacerated a repaired fibrillated tendon. Fusion of the shoulder would undoubtedly have been a better procedure than repair. A third had a rim rent tear of four months' duration, and, although he performs heavy labor, he has a massive defect in motion, without pain. The fourth is the only 1 of the series who remains severely crippled, with loss of motion, pain, atrophy and spasm. He is completely disabled two years postoperatively. In addition to the lesion of the shoulder, he has conversion hysteria, which perhaps in some part accounts for his disability.

Since all lacerations were made complete at the time of repair, estimations as to the result depending on the completeness of the original tear have not been done. A comparison of cases early in the series in which transplantation was made into mild bony defects with those in which transplantation was done ¾ inch (1.9 cm.) or more downward onto the humerus shows no appreciable difference in end results. Recovery seems somewhat slower with radical transplantation. I would therefore suggest that the extent of the tear will control the extensiveness of repair (figs. 4, 5, 6 and 7). As can be seen, results are uniformly excellent except when there are rim rent tears or badly fibrillated tendons or when a neurosis exists.

C. *Musculotendinous Separation of the Supraspinatus and Infraspinatus Muscles.*—No case of musculotendinous separation has been found other than the 1 originally reported. Treatment of the patient was previously reported as an early failure. On recent examination, three years postoperatively, he was seen to have a full range of motion and 75 per cent strength and to be asymptomatic. The new type of repair, apparently taking up the slack in the tendon, provided a satisfactory outcome.

D. *Calcification or Ossification of the Supraspinatus Tendon.*—Ossified tendon lesions have been encountered twice associated with calcification, and calcified tendon lesions, in 3 other instances. In each instance symptoms had been present in the shoulder for months to years, with a history of either slow onset or a direct blow on the shoulder. In no case did onset occur after an initial twisting strain, a fall on the outstretched arm or a dislocation. Symptoms varied from moderate discomfort to extreme pain, spasm and protection. This variation depended generally on whether calcified material had been extruded into the bursal sac. In each instance various modalities such as massage, diathermy

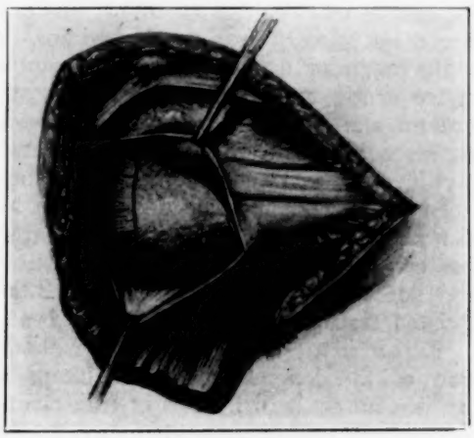


Fig. 5.—Incising the bursal roof.

and attempts at needling and washing of the calcified area or bursa had been carried out. In 1 instance the calcification was associated with laceration. Follow-up observation has been maintained in all 5 cases. One case, in which operation was done less than one month before the time of writing, is too recent for determination of results. In 3 of the other 4, recovery has been

complete and no recurrence of calcification or ossification has ensued. In 1 case of associated laceration there is still slight occasional pain, classed with the results of laceration. The speed of recovery in these cases, even when excision of ossification was done, was much more rapid than that for repair of tendon injuries caused by laceration.

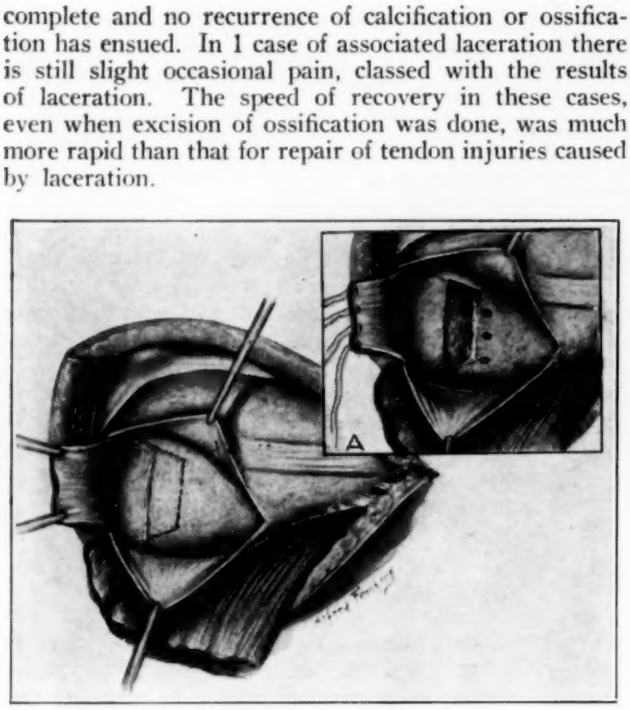


Fig. 6.—Creating a wedge-shaped defect in the area of the greater tuberosity.

E. *Lesions of the Subscapularis Tendon (Recurrent Dislocation).*—In 3 cases in which the shoulder was radically explored there was recurrent dislocation. Gross stretching of the subscapularis tendon was found but would have been missed had not the shoulder been carefully dissected. In addition to being stretched the tendon was thin throughout the portion proximal to its insertion, slightly yellowish and narrowed from above downward. The appearance was that of fibrous degeneration and repair of long standing following laceration within the tendon substance. In 1 case there was complete avulsion of the muscle and tendon substance from the anterior border of the glenoid cavity and the anterior surface of the scapula in its outer half. It is not known whether this condition was present in the other cases, since it was not looked for. On the basis of the foregoing data I suspect that recurrent dislocation frequently may be associated with stretching or laceration and fibrous repair of the subscapularis tendon plus avulsion from the under surface of the scapula in its outer part and from the rim of the glenoid cavity. In all the cases mentioned repair was by transplantation of the attachment of the subscapularis tendon to a new bony defect created in the humerus ¾ inch (1.9 cm.) lateral to the bicipital grove. In 2 there was an associated transplantation of the long head of the biceps. Repair in the other was done without transplantation of the long head of the biceps, as this structure was absent. In 2 cases of transplantation of the subscapularis tendon more than two and one-half years have passed without redislocation. The third case is too recent for follow-up study.

3. BURSAL LESIONS

A. *Obliterative Subacromial Bursitis (Frozen Shoulder).*—Seven patients with this lesion were operated on. All had previously received extensive conservative treatment. All had a lesion massively obliterated by dense adhesions requiring sharp dissection throughout most or all of their extent. Adhesions ordinarily were found to be unusually dense about the subscapularis tendon. The course of 2 patients could not be followed. One was treated too recently to be reported on. The 4 others of the 7 show a complete range of motion and complete absence of pain or other symptoms, except that 1 states that in bad weather he still has a twinge of pain. After division of adhesions in the subacromial area and manipulation to stretch or destroy adhesions about the subscapularis tendon, the arm was supported in abduction for an average of six weeks in a plaster spica. Prolonged physical therapy was necessary after release from the plaster.

B. *Laceration of the Bursal Floor Without Tendinous Involvement.*—This has been observed only once and carried with it symptoms of mild tendon laceration. Replacement of the bursal floor gave rapid relief of symptoms and brought about complete recovery.

4. LESIONS OF BONE

A. *Sharp Exostosis at the Tendinous Attachment of the Greater Tuberosity.*—The patient with this lesion, previously reported on, who was treated by exostosectomy done beneath the periosteum and the bursal floor, has been followed to date and shows complete recovery, although two years ago I granted him a result only 75 per cent satisfactory.

B. *Rounded Exostosis on the Greater Tuberosity Associated with Tendon Laceration.*—Two patients with lesions of this type have been operated on. The history of initial injury always includes a blow on the shoulder, with a steadily increasing amount of disability generally associated with localized pain and tenderness and a decreasing range of motion. Roentgen examination at first gives negative results. Gradually there develops a calcified shadow over the anterior portion of the upper border of the greater tuberosity, increasing in size and later becoming of osseous density. One patient, observed for three and one-half years, has a 95 per cent range of motion at present, is completely asymptomatic and shows no recurrence of exostosis on roentgen examination. The other patient has been operated on within the past month, and it is of course too soon for follow-up study.

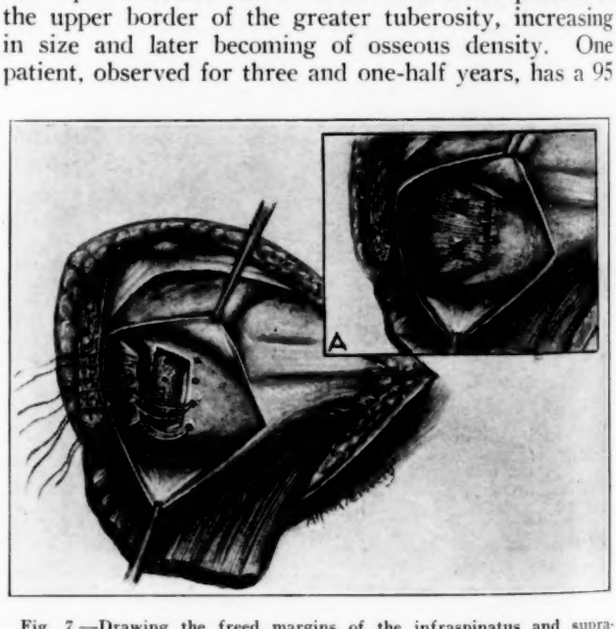


Fig. 7.—Drawing the freed margins of the infraspinatus and supraspinatus tendons down into the defect with four silk sutures.

C. *Osteochondritis.*—Osteochondritis has been encountered unsuspectedly in 2 patients whose shoulders

were massively explored. In 1, a girl of 17 who had been in a severe motorcycle accident, the lesion consisted of a small localized area of cartilaginous and bony defect not more than 0.5 cm. in diameter lying directly under the attachment of the supraspinatus tendon. The patient did not know the actual form of injury received. There was every classic symptom of a tear of the supra-

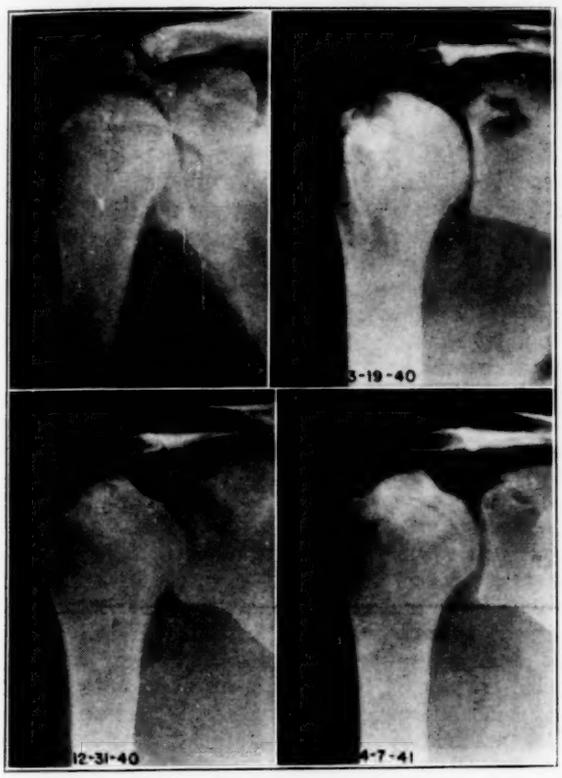


Fig. 8.—Massive osteochondritic changes not noted preoperatively, after exploration at which no pathologic condition was found, continued to progress.

spinatus tendon, including a sulcus and a prominence. At operation the tendon attachments were found normal; the osteochondritic defect was discovered and curetted; its base was drilled, and remarkably rapid recovery ensued. Though less than six months have passed after operation, there is no clinical or symptomatic defect in the shoulder. The other patient has massive osteochondritis involving practically all the articular surface of the humeral head, with faint roentgen evidence thereof which passed unnoticed preoperatively (fig. 8). Disability of the shoulder consisted mainly of loss of motion. There was an indefinite complaint of low grade continuous pain but no catch or arm drop sign. At operation no pathologic condition was found. The gradual progress of the lesion has been followed with roentgenograms. Since the education afforded by this patient, a patient with a similar condition has been observed but of course not operated on.

CONCLUSIONS

1. Radical exploration of the shoulder joint through a division of deltoid fibers close to their attachment to the acromial margin permits thorough inspection for pathologic conditions and carries with it no permanent defect so far as deltoid function is concerned.

2. The results of repair of laceration of the supraspinatus and infraspinatus tendons by transplantation can give a high percentage of success.

3. Fusion of the shoulder is indicated when complete avulsion of the tendinous cuff has occurred, massive fibrillation of a tendon is present or old crescentic tears exist.

4. Early osteochondritis of the head of the humerus may present a clinical picture difficult to differentiate from that of laceration of the short rotator tendons.

58 East Sixty-Fifth Street.

ABSTRACT OF DISCUSSION

DR. JOSEPH J. KUTLANDER, Cleveland: Best results in the treatment of shoulder disabilities and injuries depend on an accurate diagnosis of the underlying pathologic condition. In the past, most of us have been inclined to be too conservative and not explore the bursa and supraspinatus tendon. The treatment of complete avulsion of the tendons, particularly the short rotators, requires replacement by suture, usually directly to the bone. It is quite possible, however, to secure equally good results by suture of the torn tendons to the surrounding tissues in the immediate locality, that is to the periosteum, capsule or even the under surface of the deltoid with the arm held in abduction. This leads me to wonder whether this treatment isn't just as applicable to a complete avulsion of the shoulder cuff instead of performing an arthrodesis as advocated by Dr. Bosworth. Some believe that calcium deposits originate in the supraspinatus tendon through the calcification of small deposits of blood following fraying or tearing of the tendon, and that this deposit then ruptures into the subdeltoid bursa. Deposits often are visualized in both the tendon and the bursa. Which appeared first, we do not know. Removal of the calcium deposit gives dramatic relief from pain. Pain is also readily relieved by the injection of procaine and needling the tender area. Flushing the bursa with saline solution is also excellent treatment, as is the use of diathermy. Pain is often relieved with the latter modality without a diminution of the calcium, so it is often a question what really causes the pain.

DR. LAURENCE JONES, Kansas City, Mo.: I wish to call attention to a basic point in the question of shoulder joint physiology. The original article was published some eight years ago, but as it was done rather badly one cannot blame the profession for having almost forgotten it. At that time it was thought that the term "short rotators" was a misnomer. Their insertion at the extreme end of the humerus makes rotation a minor fact. In reality these are suspensory muscles attached at three points. In front there is the subscapularis, above is the supraspinatus, and posteriorly the tendinous fusion of two muscles, the teres minor and the infraspinatus. This is a transitional joint in the weight bearing quadruped, but in the human being ordinary function is exactly the opposite, except in "pushing." It has been generally agreed that their major function is to jam the head of the humerus firmly into the joint so that the various stresses and strains of the larger muscles can be performed without dislocation or abnormal movement. The paper was enjoyed greatly but issue was taken with the idea that a shoulder should be arthrodesed as long as the short rotator suspensory muscles can be recovered. Even in rare instances in which fracture dislocations complicated by comminution of the head of the humerus exists, the head can be discarded and the suspensory muscles retained and reimplanted in the shaft. A new head forms, it will stabilize the shoulder function, and in none of my own cases or in cases of other physicians using this technic has dislocation occurred. Many of these cases have been followed for many years.

DR. DAVID M. BOSWORTH, New York: As regards arthrodesis, it depends on what the findings were at operation. Two of these shoulders with complete avulsion of the rotator cuff showed chalky bone, and one could not fasten it back to the bony structure anywhere. The cuff was not long enough to fasten to the soft tissues. Two of them were old cases of avulsion of the cuff, in which the cuff had retracted over a period of four months or a year. It was impossible to get it back satisfactorily in approximation to the point of avulsion. Not only that, but massive fibrosis and loss of bursa itself forecast a poor outcome. In those cases I would advise doing an arthrodesis. As to rotators versus suspensories: I believe that

these tendons are rotator tendons. They rotate the head of the humerus and the rest of the upper extremity. If you will notice, there is no space between the supraspinatus and the infraspinatus at their attachment. There is a good space between the subscapularis anteriorly and the supraspinatus as well as the teres minor posteriorly and the infraspinatus. So I would group them from a three point angle. Again I would do that because in the supraspinatus and infraspinatus tendons the approximation of the head of the humerus to the under surface of the acromion process by its jamming action inhibits blood supply and repair, whereas I specifically stated that repair does occur in the tendon, anteriorly the subscapularis and posteriorly the teres minor.

TRICHINOSIS

REPORT OF NINETEEN CASES OF CLINICAL INFECTION AND TWENTY-ONE CASES OF ASYMPTOMATIC INFECTION

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Trichinosis, in spite of the fact that it is so old that it was known to the ancients, has assumed new interest in the light of many recent publications on the disease. This particular interest at present probably is the result of two factors: First, it has been claimed that in many cases trichinosis is undiagnosed by physicians and, second, it has been declared that the principal cause of the supposed increase in incidence of the disease is the ingestion by persons of meat from hogs fed on raw garbage. The first conception has been acquired through the numerous published results of routine necropsy performed at various public and private hospitals in the United States. These examinations have revealed that the percentage of infection varies from 3 to 28, depending on the geographic sector in which examinations are made.

What has not been sufficiently stressed, however, is the consideration that the percentage of infection has been determined only after examination of large quantities of those muscles (and in particular the diaphragm) which are most likely to become invaded by Trichinella spiralis. In most instances the infection has been light, and in the majority of cases only a few larvae have been discovered in the entire material examined.

What has not been sufficiently emphasized, further, is the fact that almost without exception the persons concerned in such examinations had, during life, no signs or symptoms of clinical trichinosis, and hence it must be concluded that the condition found in such investigations represented asymptomatic infection which has no significance from a clinical standpoint, unless it is that once a person is infected he or she becomes immune. If this were true, infection of such slight degree might be considered "a blessing in disguise." That such a condition of acquired immunity is not merely theoretical is attested by the experiments of McCoy,[1] as well as by other experiments conducted in laboratories at the Mayo Clinic, where it has been shown that once animals are infected it is usually impossible for them to become reinfected.

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1. McCoy, O. R.: Immunity of Rats to Reinfection with Trichinella Spiralis, Am. J. Hyg. **14**: 484-494 (Sept.) 1931.

ASYMPTOMATIC AND CLINICAL INFECTION

The fundamental difference between clinical and asymptomatic infection with T. spiralis should be apparent to all. Frequently the physician is unable to diagnose typhoid when a carrier originally becomes infected, and, similarly, the physician usually is unable to diagnose trichinosis at the time the "carrier" originally becomes infected by a few trichinous cysts. Nothing in particular would be gained by the ready diagnosis of asymptomatic trichinosis, and in fact it cannot be diagnosed clinically. Even if resort is made to the cutaneous test, the diagnosis still is uncertain. To perform a biopsy on each suspected person in order to establish the validity of the diagnosis would, of course, be ridiculous.

It has been the practice of certain nonmedical writers to take physicians to task for being unable to diagnose trichinosis, and these writers have maintained that the disease, instead of following the classic picture, frequently assumes a bizarre form. What these authors have failed to understand is that all the symptoms which the patient might have had at any time before death were not necessarily attributable to trichinosis simply because a few trichinae, thoroughly encysted, were found in the diaphragm of these patients at death. In fact, such thoroughly encysted trichinae may not have caused any symptoms at all of trichinosis per se. Although physicians may at times be vulnerable to attack for failure to diagnose more or less uncommon diseases, there is no real evidence to support the contention that the classic picture of trichinosis has changed since it was first established, and it seems unlikely, on the basis of information at hand, that clinical trichinosis (as opposed to asymptomatic trichinosis) is so frequently overlooked that an infinitely larger number of instances of the disease occurs than is diagnosed.

CAUSATIVE FACTORS IN THE INCIDENCE OF TRICHINOSIS

As far as the feeding of raw garbage to hogs is concerned, evidence is not yet at hand to justify conclusions as sweeping as those some investigators have drawn concerning the effects of such a practice in relation to the incidence of trichinosis. One of us (Magath) pointed out some years ago that the commonly accepted explanation of the transmission of T. spiralis from hog to hog by the agency of the rat could not explain the incidence of trichinosis found in hogs, and there is no question of the fact that the feeding of raw garbage to hogs does, to some extent, explain a part of the incidence of trichinosis. It has been shown beyond doubt that hogs fed on raw garbage in certain cities have a higher percentage of trichinosis than those not fed garbage in other parts of the country or than those fed cooked garbage. Yet such an observation does not entirely explain the epidemiology of trichinosis. All investigators have found that an appreciable percentage of hogs which have never been fed garbage are infected, and although the incidence of trichinosis in man might be reduced by the elimination of raw garbage as hogs' food, there would still be an appreciable percentage of hogs infected with T. spiralis coming to slaughter houses if garbage were not fed to them.

SYMPTOMS AND CLINICAL OBSERVATIONS

The symptoms and observations in a case of trichinosis vary somewhat according to the degree of infection present and the resistance of the host. The classic

picture of the disease, which is generally taught, consists of onset of from a few hours to a few days after the ingestion of the infected meat, with gastrointestinal symptoms of anorexia, nausea, vomiting, abdominal cramps and diarrhea. These symptoms are undoubtedly referable to the presence of the parasites in the digestive tract. They represent the first stage of the disease and may persist until the second week, which is the period of invasion, or the second stage. During the second stage the organism is in the blood stream and is invading the organs. Various toxic symptoms are present. Fever usually is present and may endure for a few days to six or seven weeks and may be of varying intensity. Other symptoms of a toxic state, such as chills, anorexia, lassitude, headache and weakness, often are present. Various embolic or allergic manifestations appear frequently, such as edema of the eyelids with chemosis and conjunctivitis. Various cutaneous lesions (which simulate rose spots) and subconjunctival hemorrhage may be present. Invasion of muscles is accompanied by stiffness, tenderness, pain and swelling of the muscles, at times associated with pain and difficulty in chewing, swallowing or breathing. Dyspnea may be severe as a result of diaphragmatic involvement. Other muscles, especially the flexors, usually show symptoms of involvement. The third stage, or the period of encystment of the larvae, usually begins in about six weeks and in more serious instances is characterized by anemia and emaciation. Recovery may be protracted, or the patient may succumb to some intercurrent infection such as pneumonia. Total recovery may not take place for several months after the original infection, or death may even occur during the height of the disease in the second stage. In 320 cases in which patients were observed from 1909 to 1914, Ransom [2] found that the rate of mortality was 6 per cent, and in 1,550 cases reported in the United States the rate was 16 per cent.

Among the less common or more unusual symptoms, constipation or, even more rarely, intestinal hemorrhage may be present during the first stage, the stage in which gastrointestinal symptoms appear.

During the stage of invasion certain manifestations in the central nervous system may develop. These are not so uncommon as is generally believed. Several cases have been reported in which the larvae of T. spiralis were found in the central nervous system and in the spinal fluid. Evers [3] reported a case in which the picture of toxic encephalitis and neuroretinitis was present and in which larvae were found in the spinal fluid. The patient recovered. In reviewing the literature, he found that 24 cases had been reported in which larvae were found in the spinal fluid, and he wrote that manifestations in the nervous system may not be present even in cases in which larvae are found in the spinal fluid.

Until recent years little attention has been paid to cardiovascular involvement in trichinosis, although Zenker observed the larvae in the cardiac muscle of a patient who died of the disease in 1860. Spink [4] reported 6 of 18 cases of trichinosis in which electrocardiographic changes were present, and he recorded the observations made at necropsy performed on a patient with myocarditis. The symptoms and observations of myocarditis caused by trichinosis do not vary from the symptoms of other forms of acute myocarditis.

In reference to other cardiovascular complications, Cheney [5] first reported a case in which extreme hypotension was present, and Spink and Augustine [6] found hypotension in 12 of 35 cases in which the systolic pressure was less than 100 mm. of mercury. Thrombosis and infarction may occur, and pulmonary, gastrointestinal and retinal hemorrhages are sometimes seen. McNaught [7] called attention to the presence of "splinter hemorrhages," which are sometimes seen beneath the nails of patients during the period of invasion; they probably represent an embolic manifestation.

The urinary organs seldom are involved, and albumin and casts, as sometimes observed in the urine of a patient, probably represent toxic changes.

Cutaneous manifestations more often are absent than present and may appear as a rose spot rash, scarlatiniform rash or erythema multiforme. The spleen may be enlarged. Other symptoms occasionally found include cough, signs of pneumonia and pleural effusion, vertigo and tinnitus.

DIAGNOSIS

Trichinosis must be considered as one of the possible clinical diagnoses in many cases in which the patient's condition is obscure, in view of the incidence and possible varying symptoms of the condition. A history of ingestion of raw or poorly cooked pork in the recent past and the presence of a similar illness among other members of the patient's family or community are important steps in the making of a diagnosis of the disease. The presence of certain typical symptoms, such as fever with edema of the face and eyes or muscular pains with a history of a "stomach upset" a few days before, often suggests the diagnosis. In the presence of eosinophilia, with more or less typical symptoms, the possibility of trichinosis always should be considered until it has been ruled out. Certain laboratory tests aid in the confirmation of clinical impressions; however, results of examination of the stools and blood for larvae usually are disappointing. The reliability of the cutaneous test to date is uncertain, although some investigators have reported a remarkably high value for this test. Schapiro, Crosby and Sickler [8] found the test of value in 78.9 per cent of cases in which the condition later was found to be present and in 97.8 per cent of cases in which the condition later was found not to be present. The presence or absence of the disease was proved by observation at necropsy. In 400 cases of routine necropsy, Schapiro, Crosby and Sickler found that the reaction to the cutaneous test during the lives of the patients had been positive in 18.25 per cent; the cutaneous test had failed to detect the presence of the parasite in 2 instances, and of 73 cases in which a positive reaction to the test had been obtained there was in 3 no evidence of trichinosis at necropsy. False positive reactions and false negative reactions exist; the reaction to the test becomes positive in about the second week of the disease, and a positive reaction to the test can be obtained from patients years

2. Ransom, cited by Anderson, A. W.: Report of Forty-Six Cases of Trichiniasis, Nebraska M. J. **19:** 379-382 (Oct.) 1934.

3. Evers, L. B.: Manifestations of Trichiniasis in the Central Nervous System: Report of a Case with Larvae in the Spinal Fluid, Arch. Int. Med. **63:** 949-956 (May) 1939.

4. Spink, W. W.: Cardiovascular Complications of Trichinosis, Arch. Int. Med. **56:** 238-249 (Aug.) 1935.

5. Cheney, Garnett: Sporadic Trichinosis with Exereme Hypotension, J. A. M. A. **86:** 1004 (April 3) 1926.

6. Spink, W. W., and Augustine, D. L.: The Diagnosis of Trichinosis, with Special Reference to Skin and Precipitin Tests, J. A. M. A. **104:** 1801-1805 (May 18) 1935.

7. McNaught, J. B.: The Diagnosis of Trichinosis, Am. J. Trop. Med. **19:** 181-192 (March) 1939.

8. Schapiro, M. M.; Crosby, B. L., and Sickler, Margaret M.: The Correlation of Clinical Diagnosis and Postmortem Findings in Trichinosis, J. Lab. & Clin. Med. **23:** 681-687 (April) 1938.

after infection has taken place. The blood precipitin test, although confirmatory, seems to be less reliable than the cutaneous test. Positive results of biopsy on muscle constitute conclusive evidence of the disease. The specimen should be examined by the press preparation method and not sectioned. Negative results of biopsy do not entirely exclude the presence of the disease, for in its early stages, before the arrival or encystment of larvae in the muscles, it is not possible to detect evidences of it in the muscles, and in other cases the specimens for biopsy must be obtained from muscle most likely to harbor the parasite. At the Mayo Clinic it has been found that the pectoralis major muscle in that portion of it which lies in the anterior axillary line is the most reliable site for the detection of possible infection, although in the presence of a light infection, or if only superficial search is made, results of biopsy of sections from this site may be falsely negative. Rarely is the opportunity at hand to obtain sufficiently large specimens to make use of digestive methods of search for the parasite.

Patients may present one or more of the numerous symptoms, with other symptoms either absent or seemingly insignificant. Patients may be encountered who have gastrointestinal symptoms during the first stage of the disease, at which time an interesting and difficult diagnostic problem is presented. On the other hand, gastrointestinal symptoms often are absent throughout the entire course of the disease. Frequently muscular aches and pains are outstanding; again, only fever seemingly is present, in which case it is exceedingly difficult to arrive at the correct diagnosis. Patients often are seen first by ophthalmologists because in some cases ocular symptoms are predominant; in other cases the otorhinologist sees the patient because the patient complains of headache and edema of the face. Cardiac, meningeal or cerebral symptoms may obscure the entire picture. When eosinophilia is present, trichinosis must be considered, but the physician must also consider various allergic conditions, angioneurotic edema, familial eosinophilia, periarteritis nodosa and leukemia. The diseases more commonly mistaken for trichinosis are influenza, rheumatic fever or arthritis, fibrositis, sinusitis, typhoid, acute nephritis and angioneurotic edema. Many others could be included.

TABLE 1.—*Trichinosis: Symptoms and Observations in Nineteen Cases of Clinical Infection*

Symptom	Number	Percentage
General toxic	17	89
Fever	14	74
Chills	3	16
Headache	5	26
Muscular pains	17	89
Gastrointestinal	12	63
Edema	13	68
Face	13	68
Elsewhere	4	21
Ocular	10	53
Cutaneous manifestations	4	21
Central nervous system	2	11
Respiratory	2	11
Cardiovascular	0	0
Epistaxis	1	5
Menstrual	1	5
Significant loss of weight	2	11

ANALYSIS OF CASES

In 40 sporadic cases in which the diagnosis of trichinosis was made at the Mayo Clinic, exclusive of those in which the diagnosis was made at necropsy, the diagnosis was proved by positive results from biopsy of specimens of muscle or by a typical clinical history and symptoms and in a few instances by the support of a positive reaction to the cutaneous test.

Asymptomatic Infection.—Of the 40 cases mentioned, the diagnosis was made incidentally in 21 during routine examination of surgical pathologic material, and in none of these 21 cases had illness referable to trichinosis been suggested at any time previously. In 12 cases the parasite was found in muscle during routine examination of tonsils, in 2 it was found during examination of thyroid tissue, in 4 it was found during examination of tissue from the lips, in 1 in a mass in the biceps, in 1 in a specimen of lumbar muscle removed at nephrectomy and in 1 in muscle overlying a cyst of the jaw. These evidently represented asymptomatic infection only.

Clinical Infection.—In the remaining 19 cases, the patients came to the clinic with trichinosis as the cause of their symptoms. The average age of the patients was 38; the youngest was 15 and the oldest was 63. Distribution by sex was approximately equal: 9 patients were males, and 10 were females. All but 1 had been born in the United States, and the majority lived in the Middle West. Seven patients were housewives, 3 were farmers, 3 held executive positions, 2 were students, 1 was a physician, 1 was a laborer and 1 was a mail carrier.

Specific Complaints: For 5 patients the immediate complaint referred to the gastrointestinal tract; usually it was diarrhea. Three complained more of generalized aches and pains; 3 complained of ocular edema, and 2 others had first sought medical advice because of ocular symptoms, namely pain in the eyes and the sensation expressed as "tired eyes" respectively. Three complained chiefly of toxic symptoms such as fever, weakness and headache, and 1 had swollen legs. Two patients in this series of 19 presented other complaints not referable to trichinosis: 1 had a hernia and 1 had a corneal ulcer.

Eleven of the 19 patients who had clinical infection gave a history of ingestion of poorly cooked pork a short time before the onset of the illness. Five patients stated that other persons living in the same locality had symptoms similar to theirs.

General Complaints: The most common symptoms of the group were those of general toxemia, with fever, chills, perspiration, weakness, malaise or headache (table 1). Seventeen patients presented one or more of these symptoms: 14 had fever of varying degree at one time or another, only 3 gave a history of chills and 5 complained of headache. Other common symptoms were muscular pains and tenderness, complained of by 17 patients. These pains were usually general, although they were more severe in the muscles of the extremities and the back of the neck. Gastrointestinal symptoms were complained of by 12 patients, diarrhea by 8, nausea or vomiting by 6 and abdominal pain by 3. Thirteen patients had edema of the face or eyes, and 4 of these also complained of edema elsewhere: 2 of swelling of the neck, 1 of swelling of the hands, and 1 of swelling of the ankles.

Ocular symptoms other than orbital edema were found in 10 cases in this group of 19. These included photophobia, difficulty in focusing, pain in the eyes, pain on movement of the eyes, "tiredness" of the eyes and dimness of vision. One patient presented a subconjunctival hemorrhage and 1 had a retinal hemor-

rhage. One patient complained of diplopia when his eyes were tired, and his wife had noticed that he had strabismus on numerous occasions.

Only 4 patients exhibited any kind of cutaneous manifestations. One had an itching rash of the forearms and feet, 1 presented desquamation of the skin of the arms and legs, 1 had "hypersensitive" skin and 1 had general pruritus.

Involvement of the central nervous system was rare in the group of 19 cases of clinical infection. It was found in only 2 cases. One patient, encountered in the chronic stage of the disease, stated that he had been left with weakness of the right side of his body and had difficulty in walking and writing because of this weakness. His bank had refused to accept his checks because his signature had changed until he explained the situation. At the time of examination nothing was found regarding the hemiparesis. One patient presented severe stiffness and soreness of the muscles of the neck and severe vertigo with repeated vomiting. Acute otitis media had developed, however, and the patient's vestibular symptoms may well have been referable to this condition. It is interesting that this patient's condition had first been diagnosed as "encephalitis" and also that the results of examination of the spinal fluid were negative.

Two of the 19 patients who had clinical infection had respiratory symptoms; 1 of these had a persistent cough. Two had basal pulmonary rales and 1 had mild dyspnea and discomfort on deep breathing. No cardiac manifestations were found in the present series. One patient had a bloody nasal discharge and hematemesis; 2 had significant losses in weight, 1 losing 70 pounds (31.8 Kg.) in one month of illness. One patient suffered from hypomenorrhea on one occasion. Examination of the urine of 1 patient who had considerable frequency of urination gave only minimal results. There was no mortality in this group.

Reinfection: Two of the series of 19 patients with clinical infection serve to raise the question of repeated infection. Such an occurrence would be difficult to prove, because we saw the 2 patients concerned on only one occasion. In both instances the diagnosis was made by means of the clinical picture, the presence of eosinophilia and positive results of a biopsy of specimens of muscle. One of the 2 patients was a woman aged 38, a physician, who complained of fever, malaise, muscular aches and orbital edema. She had had identical symptoms on six different occasions during the ten years prior to her coming to the clinic. Results of examination of the urine had always been negative. The second patient, a woman aged 30, complained of generalized muscular aching, orbital edema and fever that had appeared intermittently during the five years prior to her coming to the clinic. She gave a history of having eaten large amounts of pork.

Laboratory Observations: The highest total leukocyte count in this series of cases was 40,000 per cubic millimeter of blood, obtained in 2 cases; the lowest was 6,100 per cubic millimeter of blood. In 10 cases there was a total leukocyte count of 10,000 per cubic millimeter of blood or less. The significance of this will be considered later in this paper. A differential count was obtained in 18 of the 19 cases of clinical infection (table 2), and the highest eosinophil count was 63 per cent, the lowest being 12 per cent. In the greatest number of cases (8) the eosinophil count was distributed between 30 per cent and 50 per cent; in 7 cases it was distributed between 10 per cent and 30 per cent, as indicated in table 2. The total erythrocyte count and hemoglobin content were of no significance. In a few cases there was a mild degree of secondary anemia.

In 7 cases there was albuminuria of grade 1 plus, and in 1 albuminuria of grade 1 to 2 plus. The results of other laboratory studies, except those of the cutaneous test and of biopsies of muscle, were of no significance.

Cutaneous tests were made in only 3 cases, and the results in each case were positive. In 2 cases positive results were obtained with a dilution of 1:10,000; in 1 case positive results were obtained with a dilution of 1:1,000. The latter case was later proved to be an instance of trichinosis by a biopsy done on muscle. In 1 case a cutaneous test was made three years after infection and the reaction was negative.

A biopsy on muscle was performed in 10 of the 19 cases of clinical infection. A positive result was obtained in 8 of the 10; in 1 other case acute myositis was present. One specimen of tissue obtained from the sternomastoid muscle and studied only by the section method apparently contained no evidence of T. spiralis. In this case and in the case of acute myositis, the clinical picture was sufficiently typical to permit a positive diagnosis to be made. In 1 case negative results were obtained when a biopsy was done on tissue taken from the calf muscle, but positive results were obtained when tissue from the pectoralis major muscle was subjected to biopsy. In the majority of cases specimens for biopsy were taken from the pectoralis major muscle, in the anterior axillary line.

TABLE 2.—*Trichinosis: Eosinophil Determination in Eighteen of Nineteen Cases of Clinical Infection.*

Determination, Percentage	Number of Cases
60 to 70	1
50 to 60	2
40 to 50	4
30 to 40	4
20 to 30	2
10 to 20	5
0 to 10	0

Diagnostic Considerations: In the majority of the 19 cases of clinical infection the presence of eosinophilia was the greatest single factor to suggest the correct diagnosis. In a few cases (6) the diagnosis was suggested before the return of the differential blood cell count. A study of the original diagnosis in these 19 cases is interesting. It had been made by either the referring physician or the physician in the Mayo Clinic who originally saw the patient. Among such diagnoses trichinosis was mentioned six times, nephritis was noted twice, indeterminate diarrhea was recorded twice, unstated infectious processes were mentioned twice and conjunctivitis, sinusitis, traumatic headache, secondary anemia, encephalitis, neurosis and migraine were noted once each.

COMMENT

Asymptomatic Infection.—In 21 cases of asymptomatic infection in which the causative organism of trichinosis was discovered during routine examination of surgical pathologic material, the same principle was present as that which is present in routine examination of tissue at necropsy. In none of these cases could the diagnosis of trichinosis as a previous illness be made

before or after the examination. Therefore, the infection must have been accompanied by few, if any, symptoms, or it must have been decidedly atypical. The extremely high incidence of positive results obtained at necropsy at first seems alarming, especially in view of the few instances in which trichinosis was diagnosed clinically; but on further analysis it would be found that the majority of patients probably had had few or no symptoms, and in such circumstances the diagnosis of illness itself would be impossible. Certainly, making the diagnosis of trichinosis would be unjustified. The infective condition in these cases has been called "asymptomatic infection" as differing from "clinical infection." In many respects asymptomatic infection is similar to primary pulmonary tuberculous infection, which also is seldom clinically diagnosed but is often discovered by a Ghon lesion which is visualized in roentgenograms of the thorax or which is revealed by the reaction to the tuberculin test. Nevertheless, the high incidence of the disease as demonstrated in cadavers stresses the need for consideration of improved public health control and education of the people.

Clinical Infection.—The symptomatologic aspects and the observations made in the 19 cases of clinical infection in this series need little comment. The more classic symptoms predominated, although cutaneous manifestations were few. A reasonable number of more "unusual" symptoms was presented, but no cardiac manifestations were found.

The total leukocyte count was normal in about half of the cases, probably because a few of the patients were first referred to the clinic after the most acute symptoms of the disease had subsided. All patients who had clinical infection presented eosinophilia, which persisted longer than leukocytosis.

In the 2 cases in this series in which reinfection was suggested, the question of acquired immunity in man is raised. A few cases of second and third infection have been reported, and recently Kaufman [9] and Lehrfeld and Breisacher [10] presented cases of second infection. The presence of immunity in man is only suggested by experimental studies with animals. The degree of immunity apparently may decrease with the passage of time. Rats seem to have a degree of natural immunity, and Roth [11] showed that partial immunity may be acquired in the more susceptible guinea pig. However, McCoy's [12] attempts to demonstrate similar immunity in 12 monkeys were not uniformly successful, although in 5 there was some evidence of partial immunity.

SUMMARY AND CONCLUSIONS

In an analysis of 19 cases of clinical trichinosis and 21 cases of asymptomatic infection incidental diagnoses were made during routine examination of surgical pathologic material. Included in the series are 2 cases suggestive of repeated infection.

Asymptomatic infection with T. spiralis and clinical trichinosis are two conditions which should be clearly separated.

9. Kaufman, R. E.: Trichiniasis: Clinical Considerations, Ann. Int. Med. **13**: 1431-1460 (Feb.) 1940.

10. Lehrfeld, Louis, and Breisacher, C. F.: A Case of Trichinosis Presenting Chemosis of the Bulbar Conjunctiva, J. A. M. A. **115**: 1794-1795 (Nov. 23) 1940.

11. Roth, Hans: Experimental Studies on the Course of Trichina Infection in Guinea Pigs: III. Immunity of Guinea Pigs to Reinfection with Trichinella Spiralis, Am. J. Hyg. (Sect. D) **30**: 35-64 (Sept.) 1939.

12. McCoy, O. R.: Experimental Trichiniasis Infections in Monkeys, Proc. Soc. Exper. Biol. & Med. **30**: 85-86 (Oct.) 1932.

THE INTRAVENOUS USE OF VITAMIN K

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The intravenous use of a vitamin K active substance in prothrombin deficient patients was first reported by Smith, Ziffren, Owen and Hoffman [1] in 1939. Phthiocol (2-methyl-3-hydroxy-1, 4-naphthoquinone), synthesized by Anderson and Newman [2] sixteen years earlier, was used. Forty-five cc. of a 0.2 per cent solution given in divided doses was sufficient to raise the prothrombin level in 1 case from 39 to 75 per cent in twenty-four hours. In other cases it was found effective in doses of 40 to 100 mg.[3] No toxic effects were observed.

Subsequently Butt, Snell and Osterberg [4] reported the effective administration of the same material in 9 cases of hypoprothrombinemia. They found that a dose of 25 mg. was not adequate but that 50 mg. brought the prothrombin to a safe level. Later, Butt, Snell, Osterberg and Bollman [5] found that 1,4-dehydroxy-2-methyl-3-naphthaldehyde was effective in 8 cases in which the material was given intravenously in doses as small as 10 mg. A compound whose exact composition was not known but was "thought to be a sodium salt of 3-sulfonic acid of 2-methyl-1,4-naphthoquinone" was effectively used intravenously in 9 cases. Menadione (2-methyl-1,4-napthoquinone) was also "administered intravenously in doses of 1 mg. suspended in sterile, physiologic solution of sodium chloride. It was effective in the few instances in which it was tried in reducing the elevated prothrombin clotting time."

Dam, Tage-Hansen and Plum [6] adminstered emulsions of vitamin K_1 to 2 infants showing hypoprothrombinemia. The prothrombin level of 1 came to normal after this treatment, and of the other, who had icterus neonatorum, "the blood picture improved slowly." The authors say "When one compares the patient's blood regeneration with that of his twin brother, who was not treated with vitamin K, it appears as though the improvement was independent of the treatment."

INDICATIONS

The cases in which the intravenous administration of vitamin K is indicated fall into three main groups:

The first group includes cases in which the preparation cannot be given orally, particularly after operations when, because of nausea, some patients cannot retain the material. Fat-soluble preparations in cases of obstructive jaundice require the administration of bile or related materials, and these often result in gastric irritation or contribute to nausea already present. The vitamin is rapidly absorbed, however, and if it can

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Dr. H. P. Smith and his associates at Iowa City gave help and suggestions in the use of their two stage prothrombin determination in this laboratory and in the intravenous use of certain of the synthetic compounds.

1. Smith, H. P.; Ziffren, S. E.; Owen, C. A., and Hoffman, G. R.: Clinical and Experimental Studies on Vitamin K, J. A. M. A. **113**: 380-383 (July 29) 1939.

2. Anderson, R. J., and Newman, M. S.: The Synthesis of Phthiocol, the Pigment of the Human Tubercle Bacillus, J. Biol. Chem. **103**: 405-412 (Dec.) 1933.

3. Cited by Brinkhous, K. M.: Plasma Prothrombin: Vitamin K, Medicine **19**: 329-416 (Sept.) 1940.

4. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: Phthiocol: Its Therapeutic Effect in the Treatment of Hypoprothrombinemia Associated with Jaundice: A Preliminary Report, Proc. Staff Meet., Mayo Clin. **14**: 497-502 (Aug. 9) 1939.

5. Butt, H. R.; Snell, A. M.; Osterberg, A. E., and Bollman, J. L.: Treatment of Hypoprothrombinemia: Use of Various Synthetic Compounds Exhibiting Antihemorrhagic Activity (Vitamin K_1 Activity), Proc. Staff Meet., Mayo Clin. **15**: 69-73 (Jan. 31) 1940.

6. Dam, Heinrik; Tage-Hansen, Erik, and Plum, P.: Vitamin K in Normal and Sick Infants, Lancet **2**: 1157-1161 (Dec. 2) 1939.

be retained for thirty minutes the depressed prothrombin will often rise to a safe level.

The second group includes cases in which the vitamin is poorly absorbed from the gastrointestinal tract. Cirrhosis of the liver with hepatic insufficiency, often accompanied by cardiac insufficiency, ascites and edema of the bowel, is one of the best examples of this type of case. Cases of chronic diarrhea, intestinal fistula and ulcerative colitis usually respond to the oral administration of the vitamin, but in occasional cases its parenteral use will be required to bring the prothrombin level to normal or near normal.

The third main group includes those cases in which the response of a damaged liver to vitamin K is to be used as a measure of hepatic function. In such cases it is desirable to control the exact amount of material that gets into the blood stream. This is a study in itself and will be discussed in a separate report.

PREPARATIONS AND METHODS USED

Since MacCorquodale and his associates,[7] Almquist and Klose,[8] and Feiser[9] almost simultaneously reported the structure of an active antihemorrhagic principle in alfalfa to be 2-methyl-3-phytyl-1, 4-naphthoquinone (vitamin K_1), a number of related compounds have been synthesized and studied for vitamin K activity. Of these, the most active studied up to the present would appear to be menadione (2-methyl-1, 4-naphthoquinone),[10] even more active than the original vitamin K_1. It is being used orally in cases of hypoprothrombinemia but has been considered too insoluble to be of practical use intravenously.

In this study, a number of different clinical conditions showing hypoprothrombinemia were included, those of obstructive jaundice predominating. Prothrombin levels were determined by the quantitative two stage method of Warner, Brinkhous and Smith,[11] which has a usual error of 3 per cent or less. On days when the atmospheric temperature is higher than 95 F. the error may go as high as 9 per cent. Determinations made on such days have not been included here.

Five different intravenous preparations were studied, and from the accompanying table it can be seen that all the compounds showed vitamin K activity. Patients with severe damage to the liver, such as cirrhosis, did not respond well to any of the preparations. The relative potency of the various materials was not studied, but rather an attempt was made to give more than adequate doses to determine the clinical effectiveness of the compounds. The results would indicate that 4-amino-2-methyl naphthol hydrochloride, 2-methyl-1, 4-naphthohydroquinone 3 sodium sulfonate, 2-methyl-1, 4-dihydroxynaphthalene diphosphoric acid ester tetra sodium salt and menadione[12] may be of practical clinical use. Two of the 3 patients receiving phthiocol[13] were suffering from severe hepatic damage, and results from this study as to the drug's vitamin K activity are inconclusive. The reports of Smith, Ziffren, Owen and Hoffman[1] and of Butt, Snell and Osterberg[4] indicated that the effective dose is rather large for its practical use, particularly since related compounds are effective in smaller doses.

Menadione has been considered too insoluble to be of use clinically by the intravenous route. The potency of the material in solution is significantly impaired by sterilization with steam at 15 pounds pressure for thirty minutes.[14] We have prepared a 0.01 per cent solution in quadruple distilled water, heated for twenty-five minutes in a boiling water bath to insure sterility. The crystals go into solution during the first few minutes of heating, and subsequent variations in temperature down to —35 C. do not precipitate the crystals. A 0.02 per cent solution may be similarly prepared and is stable over long periods if kept under negative pressure at room temperature. At atmospheric pressure it is stable if kept at not below 30 C. In this more concentrated solution the material may precipitate as crystals when kept at room temperature and atmospheric pressure. For general clinical use the 0.01 per cent solution is preferred. Both concentrations have been used for the past twenty months with results shown in the accompanying table. Doses as small as 0.1 mg. have been followed by an elevation of prothrombin levels to normal. The average minimum effective dose for patients with lowered prothrombin levels and comparatively normal liver function is yet to be determined.

A number of workers[15] have reported the instability of the vitamin K active principle on exposure to light, and our studies have confirmed this. Exposure of a solution of menadione to sunlight for fifteen minutes or less or to ordinary laboratory light for two days results in a clouding of the solution.

ROLE OF BILE SALTS

Warner and Flynn[14] have shown that water-soluble vitamin K active compounds are effectively absorbed from the gastrointestinal tract of rats rendered hypoprothrombinemic by ligation of the common bile duct. Smith and Owen[16] demonstrated the utilization of similar substances in cases of obstructive jaundice presenting lowered prothrombin levels. In none of the cases were bile salts or bile given. These results support the conception that the chief role of bile or of bile salts is to render the fat-soluble preparations of vitamin K available to the intestinal mucosa for proper absorption. In our cases bile salts were not given orally in conjunction with the intravenous injections of the vitamin K active substances, and the results would indicate that they were unnecessary. Several patients with cirrhosis received daily doses (except on Sundays) of the sodium salt of dehydrocholic acid (decholin sodium[17]) over a period of three months, along with vitamin K given intravenously. No additional rise in prothrombin levels was found. This study will be reported at a later date. In this connection it is interesting to note that one of the patients with cirrhosis receiving daily doses

7. MacCorquodale, D. W.; McKee, R. W.; Binkley, S. C.; Cheney, L. C.; Holcomb, W. F.; Thayer, S. A., and Doisy, E. A.: Identification of Vitamin K_1 (Alfalfa), J. Biol. Chem. **130:** 433 (Sept.) 1939.

8. Almquist, H. J., and Klose, A. A.: Synthetic and Natural Antihemorrhagic Compounds, J. Am. Chem. Soc. **61:** 2557-2558 (Sept.) 1939.

9. Feiser, L. F.: Synthesis of 2-Methyl-3-Phytyl-1, 4-Naphthoquinone J. Am. Chem. Soc. **61:** 2559-2561 (Sept.) 1939.

10. Almquist, H. J., and Klose, A. A.: Antihemorrhagic Activity of 2-Methyl-1, 4-Naphthoquinone, J. Biol. Chem. **130:** 787-789 (Oct.) 1939. Ansbacher, Stefan, Fernholz, Erhard, and Dolliver, M. A.: Water-Soluble Antihemorrhagic Compounds, Proc. Soc. Exper. Biol. & Med. **43:** 652-655 (April) 1940. Ansbacher, Stefan; Fernholz, Erhard, and MacPhillamy, H. B.: Natural Vitamin K and Synthetic Vitamin K, ibid. **42:** 655-658 (Nov.) 1939. Fernholz, Erhard; Ansbacher, Stefan, and MacPhillamy, H. B.: The Vitamin K Activity of Naphthoquinones, J. Am. Chem. Soc. **62:** 430-432 (Feb.) 1940. Tishler, M., and Sampson, W. L.: Antihemorrhagic Activity of Simple Compounds, ibid. **61:** 2563-2564 (Sept.) 1939. Feiser.[9]

11. Warner, E. D.; Brinkhous, K. M., and Smith, H. P.: Quantitative Study on Blood Clotting: Prothrombin Fluctuations Under Experimental Conditions, Am. J. Physiol. **114:** 667-675 (Feb.) 1936.

12. Furnished by Parke, Davis & Co., Abbott Laboratories, Hoffmann-La Roche, Inc., and E. R. Squibb & Sons, respectively. The first three products were in solution and the last product in crystalline form.

13. Dr. S. A. Anderson of New Haven, Conn., and Sharp & Dohme supplied us with this material.

14. Flynn and Warner, cited by Brinkhous.[3]

15. Almquist, H. J.: Chemical and Physical Studies on the Antihemorrhagic Vitamin, J. Biol. Chem. **117:** 517-523 (Feb.) 1937. MacCorquodale, D. W.; Binkley, S. B.; McKee, R. W.; Thayer, S. A., and Doisy, E. A.: Inactivation of Vitamin K by Light, Proc. Soc. Exper. Biol. & Med. **40:** 482-483 (March) 1939.

16. Smith, H. P., and Owen, C. A.: The Absorption of Water-Soluble Vitamin K Without the Aid of Bile Salts, J. Biol. Chem. **134:** 783-784 (July) 1940.

17. Supplied by Riedel-De Haen, Inc.

Results of Medication with Drugs Having Vitamin K Activity

Patient	Age	Diagnosis	Drug	Amount, Mg.	Initial Prothrombin Level, Percentage of Normal	Time Elapsing Between Medication and Second Prothrombin Determination	Second Prothrombin Determination, Percentage of Normal	Final Prothrombin Level, Percentage of Normal	Total Amount of Drug Given, Mg.	Time Elapsing Between Initial Dose and Final Prothrombin Determination, Days
1. J. B.	42	Cancer of head of pancreas	4-amino-2-methyl-naphthol hydrochloride	1.0	49.5	24 hours	65.2	84.9	4.0	4
2. C. B.	59	Cancer of head of pancreas	4-amino-2-methyl-naphthol hydrochloride	1.0	13.9	24 hours	22.4	99.8	13.0	12
3. A. L.	52	Cancer of head of pancreas	4-amino-2-methyl-naphthol hydrochloride	2.0	40.9	5 days	102.2	....	....	..
4. B. P.	67	Cancer of head of pancreas	4-amino-2-methyl-naphthol hydrochloride	6.0	39.0	12 days	87.3	....	....	..
5. M. M.	69	Cancer of common bile duct	4-amino-2-methyl-naphthol hydrochloride	6.0	18.4	5 days	78.1	....	....	..
6. S. V.	45	Stone of common duct	4-amino-2-methyl-naphthol hydrochloride	1.0	79.6	2 days	85.0	96.0	2.0	7
7. W. F.	63	Bleeding peptic ulcer; chronic alcoholism	4-amino-2-methyl-naphthol hydrochloride	1.0	89.5	3 days	103.2	....	....	..
8. T. L.	62	Cancer with metastases to liver	4-amino-2-methyl-naphthol hydrochloride	3.0	64.9	3 days	86.0	....	....	..
9. E. S.	40	Multiple bruises; postoperative bleeding	4-amino-2-methyl-naphthol hydrochloride	1.0	85.0	15 minutes	97.3	....	....	..
10. T. W.	53	Bleeding peptic ulcer	4-amino-2-methyl-naphthol hydrochloride	16.0	78.0	10 days	94.0	....	....	..
11. M. I.	61	Stone of common duct	2-methyl-1,4-naphtha-hydroquinone-3-sodium sulfonate	4.0	28.0	2 days	66.7	70.7	10.0	5
12. G. J.	28	Stone of common duct	2-methyl-1,4-naphtha-hydroquinone-3-sodium sulfonate	2.0	95.4	24 hours	91.0	....	....	..
13. W. P.	41	Stone of common duct	2-methyl-1,4-naphtha-hydroquinone-3-sodium sulfonate	2.0	84.7	3 days	108.3	....	....	..
14. A. S.	74	Cancer of head of pancreas	2-methyl-1,4-naphtha-hydroquinone-3-sodium sulfonate	2.0	45.4	24 hours	80.4	93.4	10.0	8
15. Z. J.	45	Bacterial endocarditis	2-methyl-1,4-naphtha-hydroquinone-3-sodium sulfonate	2.0	71.0	20 hours	90.2	....	....	..
16. F. L.	61	Cancer of rectum	2-methyl-1,4-naphtha-hydroquinone-3-sodium sulfonate	2.0	75.6	24 hours	89.1	....	....	..
2. C. B.	59	Cancer of head of pancreas	2-methyl-1,4-dihydroxy naphthalene diphosphoric acid ester tetra sodium salt	100.0	72.2	9 days	89.6	....	....	..
17. O. H.	63	Obstructive jaundice (stone of common duct ?)	2-methyl-1,4-dihydroxy naphthalene diphosphoric acid ester tetra sodium salt	10.0	88.2	24 hours	103.2	....	....	..
18. H. K.	69	Cancer of head of pancreas	2-methyl-1,4-dihydroxy naphthalene diphosphoric acid ester tetra sodium salt	20.0	66.5	7 days	89.7	....	....	..
19. C. P.	63	Cancer of head of pancreas	2-methyl-1,4-dihydroxy naphthalene diphosphoric acid ester tetra sodium salt	10.0	82.6	19½ hours	108.3	....	....	..
20. L. T.	61	Cancer of head of pancreas	2-methyl-1,4-dihydroxy naphthalene diphosphoric acid ester tetra sodium salt	10.0	83.4	2 days	91.1	....	....	..
21. J. S.	82	Thrombopenia	2-methyl-1,4-dihydroxy naphthalene diphosphoric acid ester tetra sodium salt	10.0	81.2	24 hours	87.5	....	....	..
22. W. E.	47	Alcoholic cirrhosis	Phthiocol	400.0	77.5	4 days	80.0	....	....	..
23. E. W.	36	Ulcerative colitis	Phthiocol	150.0	88.8	11 days	109.5	....	....	..
24. J. N.	54	Alcoholic cirrhosis	Phthiocol	200.0	58.0	4 days	67.8	....	....	..
25. H. B.	49	Stone of common duct	Menadione	4.0	5.9	24 hours	48.0	105.1	22.0	11
26. H. B.	59	Cancer of head of pancreas	Menadione	2.0	83.5	2 hours	92.2	106.0	2.0	3
27. E. F.	77	Stone of common duct	Menadione	1.0	69.0	24 hours	81.2	....	....	..
28. E. J.	69	Stone of common duct	Menadione	1.0	80.7	4 hours	105.0	....	....	..
29. R. D.	51	Cholelithiasis	Menadione	2.0	87.4	3 days	96.0	....	....	..
30. A. L.	57	Cancer of common bile duct	Menadione	0.5	38.8	4 days	69.5	81.7	2.5	6
31. A. N.	61	Stone of common duct	Menadione	1.0	88.4	20 hours	98.5	....	....	..
32. C. S.	68	Cancer of head of pancreas	Menadione	0.1	85.6	20 hours	101.0	....	....	..
33. F. Y.	57	Cancer of head of pancreas	Menadione	3.0	67.2	8 days	97.0	....	....	..

Results of Medication with Drugs Having Vitamin K Activity—Continued

Patient	Age	Diagnosis	Drug	Amount, Mg.	Initial Prothrombin Level, Percentage of Normal	Time Elapsing Between Medication and Second Prothrombin Determination	Second Prothrombin Determination, Percentage of Normal	Final Prothrombin Level, Percentage of Normal	Total Amount of Drug Given, Mg.	Time Elapsing Between Initial Dose and Final Prothrombin Determination, Days
34. W. Z.	23	Hemophilia, catarrhal jaundice	Menadione	12.0	39.7	3 days	73.8	....	....	..
35. W. J.	38	Ileostomy	Menadione	1.0	92.0	2 hours	100.8	....	....	..
36. C. N.	27	Hemorrhage following tonsillectomy	Menadione	4.0	79.0	20 hours	87.0	93.1	8.0	44 hr.
37. L. R.	26	Menorrhagia and metrorrhagia	Menadione	0.1	76 0	44 hours	99.8	....	....	..
38. N. C.	61	Cancer with metastases to liver	Menadione	2.0	88.8	2 hours	100.0	....	....	..
39. J. E.	65	Bleeding from bowel (undetermined origin)	Menadione	0.1	90.6	20 hours	101.2	....	....	..
40. R. H.	49	Alcoholic cirrhosis	Menadione	7.0	57.0	4 days	88.8	....	....	..
41. F. K.	57	Alcoholic cirrhosis	Menadione	8.0	79.5	4 days	83.4	....	....	..
42. A. L.	53	Cirrhosis of liver (undetermined origin)	Menadione	228.0	87.5	128 days	81.5	....	....	..
43. A. M.	56	Alcoholic cirrhosis Banti's disease (?)	Menadione	5.0	69.0	4 days	85.5	....	....	..
44. M. L.	30	Acute hepatitis (alcoholic)	Menadione	3.0	77.6	2 days	90.1	....	....	..
45. J. B.	34	Threatened abortion	Menadione	1.0	80.0	12 hours	90.3	....	....	..
46. U. W.	52	Myelogenous leukemia	Menadione	2.0	75.2	1 hour	82.5	....	....	..
47. M. H.	74	Myelogenous leukemia	Menadione	2.0	44.8	1 hour	46.3	....	....	..
48. J. D.	44	Bronchiectasis with hemoptysis	Menadione	8.0	82.0	2 days	99.8	....	....	..
49. P. D.	50	Nontoxic goiter	Menadione	2.0	71.0	24 hours	94.2	....	....	..
50. J. K.	52	Cancer of common bile duct	Menadione	0.25						
51. L. K.	55	Cirrhosis of liver (undetermined origin)	Menadione	166.0	56.2 60.5	15 hours 102 days	77.0 63.7	87.6	....	..
52. T. N.	54	Cirrhosis of liver (undetermined origin)	Menadione	164.0	49.3	93 days	66.2	....	....	..

of vitamin K and bile salts orally and vitamin K intravenously on two occasions in which the bile salts were discontinued showed a drop in his prothrombin level with a resumption of the tendency to bleed. The bleeding stopped and the prothrombin level returned to its former status when the bile salts were resumed. This would suggest that the patient's vitamin requirement was high and the bile salts were necessary to the proper absorption of the material taken by mouth, even though bile was present in the bowel. Or it might suggest that in certain cases of hepatic insufficiency the bile salts serve an additional function to that of aiding in the absorption of the vitamin.

In this and in 1 other case of cirrhosis there was a limited response to the oral administration of vitamin K. Subsequent intravenous therapy was followed by a prompt further elevation of prothrombin and a dramatic improvement in the clinical condition of the patient. In both cases there was advanced peripheral edema and some ascites, and it is possible that an accompanying edema of the bowel interfered with the proper absorption of the vitamin.

REACTIONS

Koller [3] gave 4 healthy persons 180 to 200 mg. of menadione by mouth. No abnormality was noted except nausea. In rabbits a dose of 30 mg. per kilogram of body weight produced no symptoms. In dogs, however, in doses of 15 to 30 mg. per kilogram given intramuscularly, menadione caused vomiting, albuminuria and porphyrinuria. Warner and Flynn [18] found that the potassium salt of the disulfuric acid ester of 2-methyl-1, 4-naphthohydroquinone was not toxic to rats in doses of one hundred times the physiologic requirements. In the present study no reactions were observed, either immediate or delayed. The material is irritating to tissues if it gets outside the vein. A total of 1,315 doses of vitamin K active substances have been administered intravenously during the past twenty months. One patient received 880 mg. of phthiocol over a period of fifty-six days and during the next five months 336 mg. of menadione. As much as 20 mg. of the latter was given in one day. Three patients received 2 mg. of menadione intravenously daily (except Sundays) over a period of three months and three days, three months and twelve days and four months and sixteen days respectively. No toxic effects were observed. The urine of the 4 receiving prolonged administration was porphyrin free.

From this study it would appear that menadione is effective in doses of 0.5 mg. or less intravenously and that this dose is well below the toxic dose of the drug.

INTRAVASCULAR CLOTTING

The question has been raised of intravascular clotting from an overdose of vitamin K. From this study there appears to be a limit to the level to which the prothrombin can be elevated, even with large doses of the vitamin. In none of the cases was there any evidence of thrombus formation. It is interesting to note in this connection that high levels of prothrombin apparently may exist without the occurrence of intravascular clotting. Prothrombin levels fluctuate widely during pregnancy. In 1 case observed in the obstetric clinic of the Presbyterian Hospital the level ran as high as 175 per cent without any abnormal condition being apparent.

SUMMARY

1. A number of synthetic compounds were administered intravenously to patients with lowered prothrombin levels, followed by an elevation of the prothrombin. No toxic effects were observed.

2. Menadione is highly active and is sufficiently soluble to be of practical clinical use.

3. In some cases in which response to the oral administration of vitamin K is poor the intravenous use may be of benefit.

4. Bile or related substances ordinarily are not required for the utilization of the vitamin when it is administered intravenously. There is some indication that certain patients may receive maximum benefit only when bile substances are used.

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18. Warner, E. D., and Flynn, J. E.: Absorption of Water-Soluble Vitamin K from Intestinal Tract, Proc. Soc. Exper. Biol. & Med. **44**: 607-608 (June) 1940.

Clinical Notes, Suggestions and New Instruments

SPECIFIC CUTANEOUS REACTIONS WITH HISTOPLASMOSIS

PRELIMINARY REPORT OF ANOTHER CASE

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Meleney's [1] recent review of histoplasmosis (Darling) listed 32 cases. Since his review 2 more cases of the disease have been reported by Brown, Havens and Magath [2] and by Rhodes, Conant and Glesne.[3] Another case, in which a patient recently admitted to St. Luke's Hospital for the diagnosis and treatment of a chronic lesion of the larynx was found to have the Histoplasma capsulatum infection, is reported here. The tissues in the lesion of the larynx had the specific structure seen in histoplasmosis. The mold was cultured from specimens taken for biopsy. Intradermal injections of filtrates of broth cultures of the fungus in the patient and in animals experimentally infected caused immediate and delayed specific cutaneous reactions.

REPORT OF CASE

A white man aged 63 had irritation of the throat and hoarseness for eighteen months, pain in the left side of his throat for seven months and a loss of 40 pounds (18.1 Kg.) in six months. He had dull epigastric distress aggravated by food but relieved by emesis, sodium bicarbonate and warm water. The symptoms increased in severity. He had dysphagia, weakness, occasional nocturnal sweats and a chronic cough. He occasionally expectorated thin sputum streaked with blood. He had had diphtheria in 1915, gonorrhea and syphilis in 1925 for which treatment had been given, pleurisy in 1932 and chronic otitis media on the left side. He had used laxatives, hydrochloric acid and patent remedies. In his youth he had been a carpenter and later a bartender.

The patient was weak, obviously had lost considerable weight and had a hoarse speech. The temperature was 98.6 F., the respiratory rate 18, the pulse rate 80 and the blood pressure 115 systolic and 75 diastolic. The eyes reacted to light and in accommodation; the mucosa of the nose was normal. The right external ear was normal; the left contained dried exudates. The teeth were in fair condition, but the gingival margins were ulcerated and bled freely. The largest of the ulcers at the base of the left first molar caused considerable discomfort and had been treated repeatedly without success.

On examination with a mirror the left true cord of the larynx was seen to have a small polypoid tumor in the midportion of the phonating edge. The aryepiglottic folds and arytenoid cartilages were thickened, and their laryngeal surfaces had a soft, slightly ulcerated mass extending across the entire posterior commissure. This lesion was red and was covered with a gray purulent secretion. The motility of the cords was impaired by the mass. There was hyperresonance of both lungs with numerous fine rales. The abdomen was soft and protuberant, and the epigastrium was definitely tender. The liver extended 3 cm. below the inferior right costal margin. The only other noteworthy physical sign was a longitudinal ridging of the finger nails and toe nails.

The Kahn reaction of the blood was negative, the urine contained nothing unusual and repeated examination of the stool and the sputum gave negative results. Biopsies done on the sternum gave negative results and differential blood stains were normal. The red blood cell count ranged from 5,120,000 on admission to 4,680,000 on Feb. 15, 1941, the hemoglobin content was 15.4 to 12.8 Gm. per hundred cubic centimeters and the leukocyte count ranged from 7,950 to 5,620 per cubic millimeter.

Roentgen examination of the larynx suggested an irregularity of the body of the thyroid cartilage and a slight increase in density about the arytenoids. The esophagus, heart and aorta showed no changes. Both lungs had increased root shadows, and there were many small calcified regions in the left hilus. The peribronchial tissues were thickened in both pulmonic fields. A complete gastrointestinal study demonstrated only decreased motility of the ileum. The liver and spleen were enlarged.

On direct examination of the larynx the day after admission the mucosa of the larynx had the usual color. A small round polyp was attached near the center of the phonating surface of the left vocal cord. This was removed and the edge of the cord straightened. A verrucous ulcerated mass extended from side to side across the posterior commissure involving the upper surface of the arytenoids and extending below the level of the two cords. It spread laterally into the ventricles and superiorly on the lateral margins to involve the posterior surface of the false cords. Tissues were removed for histologic study, and secretions were taken for bacteriologic examination.

The tissues removed were examined by Dr. Edwin F. Hirsch. A surface squamous epithelium present on some sections was regular but at other levels it was thin, and the underlying cellular stroma extended to the surface. The unusual feature of the tissues was the cellular content of the stroma. In this fibrillar tissue were lymphocytes, plasma cells and many large mononuclear phagocytes. The last-mentioned cells had an acidophilic granular cytoplasm and round vesicular nuclei with granules of chromatin. They varied in size; some were huge, and in the cytoplasm of the cells were clusters of small oval bodies with a small central mass of granular cytoplasm and a hyaline membrane. In some of the large cells the number of inclusions was so great that the cytoplasm appeared vacuolated. The growth of fibroblastic stroma in certain regions was in excess, but in this also were isolated large cells with granular cytoplasm and inclusion bodies. The inclusions were interpreted as some fungus, and the lesion was diagnosed as reticuloendothelial cytomycosis (histoplasmosis of Darling). The suggestion was made also that other tissues be removed for culture and for confirmation of the diagnosis. Accordingly by a second direct examination of the larynx Nov. 20, 1940 the previous observations were confirmed. More tissue was removed for histologic and cultural studies.

The patient had lost 10 pounds (4.5 Kg.) more since admission, and his symptoms continued. Small ulcers developed in the left premolar region of the mandible and on the right side of the tongue posteriorly from which no unsual organisms were cultured. His spleen became palpable at the costal margin, but the liver did not become larger. The temperature in the afternoon or in the evening rose to 99 or 99.6 F.

Vitamins and fluids were administered intravenously to maintain adequate nutrition. The specific therapeutic agents used were neoarsphenamine, sulfanilamide, potassium iodide, yellow bone marrow, gargles of potassium permanganate and antimony and potassium tartrate intravenously. These did not change the patient's condition. He died approximately five months after his condition was first diagnosed.

CULTURAL STUDIES

Cultures were taken of tissues removed from the larynx on November 20 and two sponges with exudates from the tissues on human blood agar, 10 per cent rabbit blood agar and Endo's agar plates, on semianaerobic and anaerobic blood slants and in broth. Two sets of plates were inoculated; one was kept at 37 C. and the other at room temperature. Growth appeared on the plates kept at 37 C. in seventy-two hours and on those kept at room temperature in five days. Fuzzy white colonies appeared, 0.5 to 1.5 cm. in diameter. They adhered closely to the medium and did not emulsify in saline solution. The colonies on dextrose agar were white; those on blood agar were reddish gray. In preparations stained by the Gram method the growth consisted of faint gram-negative filaments. In six

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Dr. Van Pernis is the John Jay Borland fellow in clinical research.

1. Meleney, H. E.: Histoplasmosis (Reticuloendothelial Cytomycosis): A Review, Am. J. Trop. Med. **20**: 603-615 (July) 1940.
2. Brown, A. E.; Havens, F. Z., and Magath, T. B.: Histoplasmosis: Report of a Case, Proc. Staff Meet., Mayo Clin. **15**: 812-816 (Dec. 18) 1940.
3. Rhodes, P. H.; Conant, N. F., and Glesne, L. R. B.: Histoplasmosis, J. Pediat. **18**: 235-241 (Feb.) 1941.

days, round chlamydospores appeared as branches of the myceliums and at the ends of hyphae. These were round or slightly oval bodies 3.9 to 10 microns in diameter. They had a thick wall and a vacuolated center. Scarlet red demonstrated the presence of globules of fat. After seven days there were ascus-like bodies as well as chlamydospores. The ascus-like bodies resembled the latter except that their outer margins had small nodes and became knotty or uneven. Globules of fat were present.

Growth in the semianaerobic and anaerobic slants and in broth appeared three to four days later than that on the aerobic plates. Subcultures were made in beef heart, brain broth and dextrose broth. Fluffy, white, ball-like colonies connected together with fine, threadlike myceliums, grew quickly in the dextrose broth. The colonies of subcultures on blood cell agar plates appeared in forty-eight hours and those on plasma agar in seventy-two hours. After four days the growths on the two were approximately equal. As the colonies grew older the chlamydospores and ascus-like bodies gradually disappeared, leaving only a mycelium.

Dextrose, lactose, sucrose, maltose, mannite, salicin, trehalose, sorbitol, arabinose, levulose, gallactose, dextrin, xylose, raffinose, inulin, litmus milk, peptone water and acetyl-methyl carbinol were not fermented. Indole was produced in the peptone medium.

A five day old culture on dextrose agar and a seven day old culture on agar were triturated in a mortar, suspended in saline solution and injected intraperitoneally into mice, rats, guinea pigs and rabbits. After two weeks the mice had no gross lesions. Stained preparations of blood and dextrose agar cultures, however, demonstrated mycelial threads and a few oval yeast forms, 2 to 4 microns in diameter, with granules and vacuoles. In subcultures, both the yeast and the mold form produced only mycelial threads. Cultures taken from the tissues of rats were sterile. Cultures taken on blood and dextrose agar of hepatic tissues from guinea pigs killed six weeks after inoculation contained the mycelial form after seven days. Tissues of the spleen and lung removed from mice had many large monocytes containing refractile coccoid bodies with a thick capsule. Some contained two or three of these refractile bodies; others had ten to twenty. Other tissues showed no changes. A few yeastlike bodies were found in the spleen and mesenteric lymph nodes of the guinea pigs. Tissues from the rats showed no changes.

CUTANEOUS TESTS

Two 250 cc. quantities of dextrose broth culture medium inoculated with H. capsulatum, one on Nov. 30, 1940 and the other on December 14, were centrifuged on Jan. 7, 1941 to remove the heavy mycelial growth. The supernatant liquid was passed through a Berkefeld W filter and then tested for sterility. The undiluted filtrate and dilutions of 1:1,000, 1:100 and 1:10 in 0.1 cc. amounts were injected intradermally into the patient with histoplasmosis and into mice inoculated with the mycelium. Cutaneous reactions were produced in all dilutions in the patient and in the inoculated mice. Control injections of these preparations in other patients and in uninfected mice gave negative results.

There were two varieties of cutaneous reactions in the patient and in the mice, an immediate and a delayed reaction. The immediate reaction appeared only with the undiluted filtrate, fifteen to thirty minutes after the injection. It consisted of a wheal 1 to 1.5 cm. in diameter with an erythematous margin 1 cm. wide. The delayed reaction, clearly visible after eighteen to twenty-four hours, was a well defined erythema and swelling of the skin. In the patient at the height of the reaction this region was 3.5 to 6.5 cm. in diameter. The reaction disappeared gradually in about six days. Intradermal injections of 0.1 cc. of dextrose broth in the patient and in human controls caused no reactions.

Filtrates of dextrose broth treated with three volumes of acetone U. S. P. yielded a flocculent precipitate. The precipitate was redissolved in a small amount of 0.9 per cent saline solution. Intradermal injections of 0.1 cc. of the solution in the patient and in infected mice also produced a typical wheal and erythema in thirty to sixty minutes. Tests on controls gave negative results.

No precipitin reactions were obtained with the patient's serum, in dilutions of 1:2 to 1:128, and the undiluted filtrate or the acetone precipitate redissolved in saline solution. Complement fixation tests using the antigens mentioned also gave negative results.

SUMMARY

H. capsulatum was cultured from material taken from laryngeal lesions, doubtless part of a more extensive infection, in a man aged 63. Broth culture filtrates of the fungus isolated from these lesions produced specific immediate and delayed cutaneous reactions in the patient and in mice experimentally infected. The specific substance responsible for the cutaneous reactions with these broth filtrates was precipitated with acetone. The flocculent precipitate was readily soluble in saline solutions.

SENSITIVITY OF PNEUMOCOCCI TO SULFAPYRIDINE: A RAPID QUALITATIVE TEST FOR RESISTANCE; CLINICAL EVALUATION OF THE PROBLEM

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Differences in the sensitivity of pneumococci to sulfapyridine have been suggested since the earliest days of its use.[1] MacLean, Rogers and Fleming [2] observed decided differences both in vivo and in vitro, and developed, as did Macleod and Daddi,[3] a strain resistant to sulfapyridine by passage of a sensitive strain through treated mice. These observations have been confirmed and extended [4] and may be summarized as follows: Pneumococci differ profoundly in their sensitivity to the sulfonamides; resistant strains occur in nature; sensitive strains may become resistant when they are exposed to the drug in either the test tube, mouse or human being; resistant strains are probably permanently resistant.

The clinical implications of these results are most grave. The rational therapy of pneumococcic pneumonia demands knowledge of the sensitivity or resistance of the organism: chemotherapy in the absence of this knowledge is analogous to serotherapy in the absence of knowledge of type. The golden opportunity to cure the patient may pass before the patient's clinical course can suggest that he is infected with a resistant strain. Present laboratory tests for fastness are research pro-

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This study was aided by a grant from the Pneumonia Fund, University of Southern California School of Medicine. The sulfapyridine powder was supplied by the Lederle Laboratories, Inc.

1. Whitby, L. E. H.: Chemotherapy of Pneumococcal and Other Infections with 2-(*p*-Aminobenzenesulphonamido) Pyridine, Lancet **1:** 1210 (May 28) 1938. Bliss, Eleanor A.; Feinstone, W. H.; Garrett, A. W., and Long, P. H.: Sulfapyridine and Sulfanilamide in Experimental Pneumococcal, Meningococcal, Welch Bacillary, and Friedländer Bacillary Infections in Mice, Proc. Soc. Exper. Biol. & Med. **40:** 619-621 (April) 1939. Schmidt, L. H., and Hilles, Carolyn: Further Studies on Therapeutic Properties of Sulfapyridine in Experimental Infections, ibid. **40:** 611-614 (April) 1939. Frisch, A. W.: Observations on Sputum from Cases of Pneumonia Treated with Sulfapyridine and Sulfathiazole, J. Bact. **41:** 80-81 (Jan.) 1941. Poston, Mary A.: A Comparison of the Therapeutic Response to the in Vitro Inhibitory Effect of Various Sulfonamide Compounds on Organisms Isolated from Patients with Bacterial Endocarditis, ibid. **41:** 81 (Jan.) 1941.

2. MacLean, I. H.; Rogers, K. B., and Fleming, Alexander: M. & B. 693 and Pneumococci, Lancet **1:** 562-568 (March 11) 1939.

3. MacLeod, C. M., and Daddi, Giuseppe: "Sulfapyridine-Fast" Strain of Pneumococcus Type I, Proc. Soc. Exper. Biol. & Med. **41:** 69-71 (May) 1939.

4. MacLeod, C. M.: Metabolism of "Sulfapyridine-Fast" and Parent Strains of Pneumococcus Type I, Proc. Soc. Exper. Biol. & Med. **41:** 215-218 (May) 1939. Long, P. H., and Bliss, Eleanor A.: Relation of Strain Resistance to Chemotherapeutic Effects of Sulfapyridine in Experimental Infections in Mice, Ann. Int. Med. **13:** 232-237 (Aug.) 1939. Schmidt, L. H., and Hilles, Carolyn: Response of Different Strains of Type I Pneumococcus to Sulfapyridine, Proc. Soc. Exper. Biol. & Med. **43:** 288-293 (Feb.) 1940. Bullowa, J. G. M.; Osgood, E. E.; Bukantz, S. C., and Brownlee, I. E.: Effect of Sulfapyridine Alone and with Serum on Pneumococcus Pneumonia and on Pneumococcus-Infected Marrow Cultures, Am. J. M. Sc. **199:** 364-380 (March) 1940. Schmidt, L. H.; Claugus, C. E., and Starks, Effie: Response of Sulfapyridine-Fast Pneumococci to Sulfathiazole and Sulfamethylthiazole, Proc. Soc. Exper. Biol. & Med. **45:** 256-259 (Oct.) 1940. Schmidt, L. H.; Sesler, Clara L., and Green, Mary: The Sensitivity of Pneumococci to Sulfapyridine as Related to the Production of Hydrogen Peroxide, J. Bact. **41:** 82 (Jan.) 1941. Ross.[7]

cedures requiring days rather than hours. There is hence an urgent clinical need for a rapid test for resistance.

Virulent pneumococci, injected intraperitoneally into mice, cause an overwhelming pneumococcic peritonitis within a few hours. This is definitely altered by sulfonamide therapy,[5] the peritoneal exudate showing few and atypical organisms. We have therefore injected the sputum of patients into treated and untreated mice, comparing their exudates at various intervals. Among the first 33 patients studied have been those representing each therapeutic category. This, and the encouraging results of the test, make it advisable to indicate our observations without awaiting the results of more elaborate studies in progress.

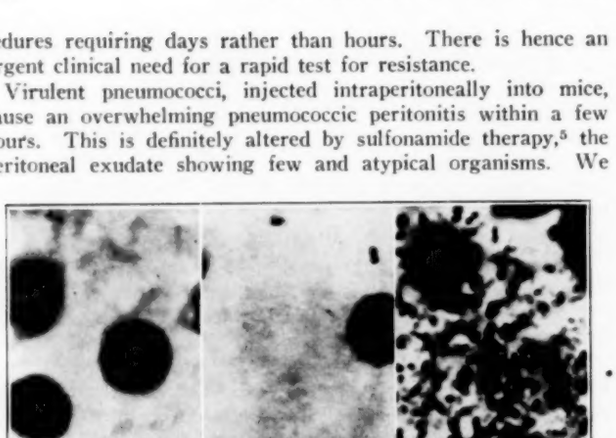

Fig. 1.—Section showing numbers of pneumococci in peritoneal exudates taken at two, eight and twenty hours from one control (upper) and one treated mouse (lower).

MATERIAL AND METHOD

The test has been run on fresh sputum or empyema pus obtained from 33 patients, representing the following types of pneumococcus: I to X, XIV to XVI, XVIII to XX, XXXI, XXXII and "no type." The sputums were those sent to the laboratory for typing, usually on admission of the patient.

Each of four mice was inoculated intraperitoneally with 0.2 cc. of 10 per cent sulfapyridine suspended in 20 per cent acacia. No further treatment was given. Sputum (or pus) was made grossly homogeneous and liquid by mixing with a minimum necessary amount of sterile saline solution. Within the first two hours after treatment the 4 treated and, in addition, 3 untreated mice were alternately inoculated with the sputum mixture, as large a volume as possible (up to 1 cc.) being used for each mouse. At various intervals thereafter peritoneal exudate was removed from each mouse and examined rapidly to determine the number and the morphology of the pneumococci. Efforts to make accurate counts were avoided. The test was read when growth of pneumococci in the untreated mice had become unquestionable (as indicated by hundreds per oil immersion field), and at no earlier time. If, at this time, the treated mice showed no increase in the number of pneumococci, or if there had been scanty growth with a preponderance of atypical forms, the strain was called sensitive; if smears of treated and control mice were virtually indistinguishable, the strain was called resistant (fast or refractory). The records were completed by subsequent smears and by observation of death, though these were not strictly a part of the test. To estimate the reliability of the test, it has been repeated a total of twenty times on three strains, 24, 60 and 100 mice respectively being used.

The results of the test were compared with the clinical records. Observations in the laboratory and in the ward were independently conducted, neither being influenced by the other.

RESULTS

Figure 1 illustrates the results of the test in the case of a typically sensitive strain. Sections of smears of exudates from 1 of the 3 control and 1 of the 4 treated mice are shown at two, eight and twenty hours after inoculation. In this case, the effectiveness of the drug is indicated by intense bacteriostasis. In figure 2 are illustrated organisms from a treated mouse inoculated with a sensitive strain, indicating the atypical structure which is sometimes observed, e. g. chaining, megacapsulation, heteromorphism and fragmentation. In the resistant strain (not illustrated), the numbers of pneumococci in treated and in control smears increase equally rapidly. In cases in which the test was repeated, complete confirmation of results was always obtained.

The total working time per test has averaged about thirty to forty minutes. The average time from inoculation to the appearance of overwhelming numbers of pneumococci in the exudate (e. g. to completion of the test) has been eighteen hours. All but three of the tests were completed between the second and the twenty-fourth hour, the other three requiring up to sixty-five hours (probably reflecting the fact that in these tests the mice received only 0.1 cc. of diluted sputum). On the average, it took more than three times as long (three and two-tenths) for the organisms to multiply profusely in treated mice as it did in the controls.

Among the 33 patients from whom specimens were obtained, the pneumococcus of one strain[6] was resistant and of the others sensitive. Two patients with sensitive strains and the one with a resistant strain failed to respond to chemotherapy, the remainder ran a satisfactory clinical course. The cases of the 3 who failed to respond are reported here:

CASE 1.—A white woman aged 28 had clinical and roengten evidence of pneumonia of the left lower lobe. She had been ill (untreated) with symptoms of pneumonia for three days; on admission her temperature was 101.4 F., her pulse rate 120 and leukocytes 24,000. Ten Gm. of sulfathiazole was given in the next thirty-two hours. At the end of this time she had, if anything, grown worse and was weak, toxic and apprehensive. Specific serum, 300,000 units of type I, was given in the next six hours, followed immediately by profound subjective and objective improvement. She was discharged well on the sixteenth day of illness. Pneumococcus type I in the admission sputum was resistant to sulfapyridine in mice.

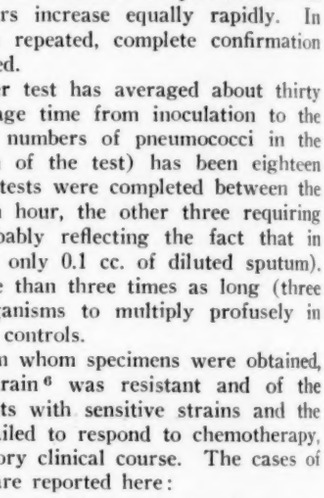

Fig. 2.—Atypical pneumococci in the peritoneal exudate of a treated mouse.

CASE 2.—A man aged 29, a Mexican, with type II pneumococcus pneumonia of the left lower lobe of four days' duration was given sulfathiazole without improvement from the fourth to the seventh day, serum (390,000 units) on the seventh day, followed by some slight improvement and the development of a positive Francis reaction,

5. Levaditi, Constantin; Vaisman, Aron, and Krassnoff, D.: Mechanism of Sulfanilamide and Its Derivatives in Experimental Pneumococcus Infections, Ann. Inst Pasteur **62**: 36-80 (Jan.) 1939. Reid, R. D.: Mode of Action of Sulfapyridine of Pneumococcus, Proc. Soc. Exper. Biol. & Med. **41**: 437-442 (June) 1939. Meyer, Fritz; Rosefield, Irving, and Taran, Albert: Mechanism of Action of Sulfapyridine: Production of Soluble Substance, Quart. Bull., Sea View Hosp. **5**: 27-39 (Oct.) 1939. Tunnicliff, Ruth: Effect of Sulfapyridine on Phagocytosis and Dissociation, J. Infect. Dis. **66**: 148-152 (March-April) 1940.

6. A second resistant strain has been recovered: pneumococcus type XV from a patient with postoperative pneumonia who has had a long, atypical and refractory course and is still under treatment, a pleural effusion having now developed.

and sulfapyridine from the eighth to the seventeenth day with very gradual improvement. Pus was now aspirated from the chest. Though they had not been able to find conclusive evidence to that effect, the staff felt that a small and hidden pocket of empyema had probably been present since early in the disease. Pneumococcus type II both in the admission sputum and in the empyema was sensitive to sulfapyridine in mice.

CASE 3.—A white man aged 64 with severe diabetes was on 60 units of insulin daily. On admission he suffered from diabetes (uncontrolled for two months), type IV pneumococcus pneumonia of three lobes (four days' duration), severe leukopenia, auricular fibrillation and congestive failure. Specific serum, sulfathiazole, rapid digitalization and suitable diabetic therapy kept him alive for five days. At autopsy, cultures taken from the affected lungs were not successful. Pneumococci in the admission sputum were sensitive to sulfapyridine in mice.

Prior to the development of this test, we saw a patient who had been treated with sulfapyridine in a desultory and vacillating manner over a period of two months. At first each exposure to the drug resulted in clinical improvement; later there was less and less response to each exposure. He was then admitted to this hospital where enormous amounts of sulfapyridine were given, producing a blood concentration of 15 mg. per hundred cubic centimeters. The blood cultures, however, remained positive, and at autopsy he was swarming with pneumococci. A pure culture was obtained and injected in various dilutions into treated and untreated mice. No difference was observed between the two groups in time or rate of mortality, and the strain was considered drug fast. The delay, difficulty and expense of this test prompted us to develop the present method.

COMMENT

The rapid qualitative test reported has been found to be simple to perform, to require an average of eighteen hours for completion (usually four to twenty-four), and to have a sharp end point. We have not yet examined other sulfonamides nor sought to make the test more quantitative, though such studies are in progress. The possibility of using an analogous method with culture medium substituted for the mouse is under examination, but we have little hope of this proving suitable.

With regard to their response to chemotherapy, patients with pneumonia fall into several categories. Patients of group A, the present majority, are infected with a sensitive strain and respond beautifully to the drug. Those of group B, also infected with a sensitive strain, respond poorly or not at all, their lack of improvement being referable to the presence of a severe concomitant disease (case 3) or to the presence of a complication of pneumonia (case 2 probably represents this group). Those of group C are initially infected with a sensitive strain which develops fastness during chemotherapy, so that a preliminary improvement is succeeded by clinical resistance (Ross [7] and probably our last case). Patients of group D are infected with a resistant strain from the first; their progress is the same as that of untreated pneumonia (except for the added hazard of injury by the drug), and effective therapy, such as serum or some chemotherapy to which the pneumococcus is sensitive, must be given as soon as possible (case 1).

It is no less important for the clinician to bear these possibilities in mind than for him to be able to secure, at the beginning of treatment, the bacteriologic information necessary to evaluate properly the progress of the case, or to alter entirely his plan of treatment if the organism is resistant.

SUMMARY

A rapid, qualitative test, based on the inoculation of sputum into treated and untreated mice, has been developed to indicate the sensitivity or resistance of pneumococci to sulfapyridine.

The clinical response of patients to chemotherapy compared with the results of the laboratory test has given encouraging results.

7. Ross, R. W.: Acquired Tolerance of Pneumococcus to M. & B. 693, Lancet **1**: 1207-1208 (May 27) 1939.

A RAPID BEDSIDE TEST FOR THE CONCENTRATION OF SULFANILAMIDE, SULFAPYRIDINE AND SULFATHIAZOLE

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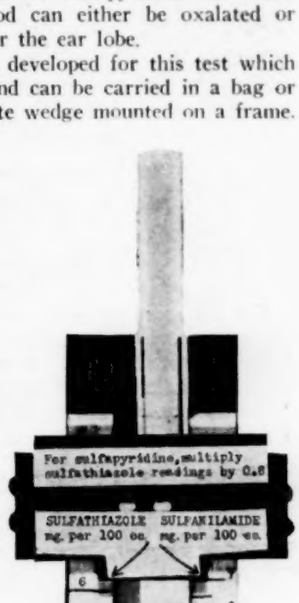
In the treatment of infectious diseases with drugs of the sulfonamide group it is desirable to maintain an optimum concentration of these drugs in the blood, and therefore periodic tests are essential for best results. The method herein described is simple and accurate and can be performed in a few minutes at the bedside or in the office. It is a modification of the Marshall method, but it has the following advantages: All reagents are stable, in tablet form. No pipets are required except one for collecting blood. Only 0.1 cc. of blood for sulfanilamide and 0.2 cc. of blood for sulfapyridine and sulfathiazole are required. The blood can either be oxalated or be obtained from the finger tip or the ear lobe.

A special colorimeter has been developed for this test which is small, compact and accurate and can be carried in a bag or in a pocket. It consists of a lucite wedge mounted on a frame. Attached to the frame is a sliding window, with an attachment to hold the test tube containing the substance to be examined. A scale attached to the frame indicates the concentration of sulfanilamide, sulfapyridine and sulfathiazole. The advantage of a lucite wedge standard is its absolute stability of color; furthermore it is unbreakable and can be made in any shade to match any color at little expense.



Lucite wedge colorimeter.

As for the test itself, the proteins are precipitated and the proper acidity obtained by means of a tablet containing sulfosalicylic and tartaric acid. The sulfonamides are then transformed into a diazo compound with a tablet containing sodium nitrite and sodium chloride. Unlike the solution of sodium nitrite used in the Marshall method, which is not stable, this reagent has not deteriorated for a period of more than two years. The excess of sodium nitrite is removed with a tablet containing sulfamic and tartaric acid. This combination is superior to a solution of ammonium sulfamate as it keeps indefinitely in dry form and also works more rapidly. The diazo compound is finally transformed into a colored compound with a tablet containing N-(1-naphthyl)-ethylene-diamine dihydrochloride which is rendered more stable in dry form by the addition of tartaric acid. The tablets are made in the proportions given in the accompanying table.

Composition of Four Tablets Used in Test

Tablet No. 1	Mg.	Tablet No. 2	Mg.	Tablet No. 3	Mg.
Sulfosalicylic acid	50	Sodium nitrite	0.3	Sulfamic acid	1.5
Tartaric acid	50	Sodium chloride	30	Tartaric acid	29
Talcum	100				

Tablet No. 4	
N-(1-naphthyl)-ethylene-diamine dihydrochloride	0.3 mg.
Tartaric acid	1.5 mg.
Sodium chloride	29 mg.

APPARATUS REQUIRED

A pipet for obtaining blood, graduated at 0.1 and 0.2 cc.; two small test tubes, 13 by 100 mm., graduated at 2 cc. and 0.95 cc.; a small funnel, 1 inch in diameter, and the colorimeter described comprise the requisite apparatus for the test.

From the Department of Medicine of the College of Medical Evangelists.

PROCEDURE

Fill test tube with water to the upper mark. Add 0.1 cc. of blood to test for sulfanilamide and 0.2 cc. of blood for sulfapyridine and sulfathiazole. Shake test tube and let stand for half a minute. Add one tablet no. 1. Shake tube and let stand for half a minute. Filter into another test tube until filtrate reaches lower mark. Add one tablet no. 2. Shake test tube and let stand for half a minute. Add one tablet no. 3. Shake test tube and let stand for half a minute. Add one tablet no. 4. Shake test tube. Insert test tube into clip of colorimeter, slide window up or down until the color of the unknown matches the lucite wedge standard and read concentration expressed in milligrams per hundred cubic centimeters of blood on the scale.

CONCLUSION

In a new, rapid, bedside method for the determination of sulfanilamide, sulfapyridine and sulfathiazole, tablets which are stable and a new microcolorimeter with a lucite wedge standard are employed.

9730 Wilshire Boulevard.

COMA FOLLOWING MEDICATION WITH TETRACHLORETHYLENE

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On the score of safety and high efficacy especially against hookworms, tetrachlorethylene (C_2Cl_4), first introduced into human medicine via the veterinary field by Hall and Shillinger [1] in 1925, enjoys great repute as approaching the ideal in anthelmintics. Its sponsors expressed the opinion that tetrachlorethylene would be found to be safer than carbon tetrachloride, a view which has been amply substantiated by later clinical experience. This is also borne out by the pharmacologic studies of Lamson, Robbins and Ward,[2] who wrote as follows: "Tetrachlorethylene differs from carbon tetrachloride in being absorbed little, if at all, in the intestinal tract of dogs in the absence of fat. If fat is present, or if enormous doses are given to animals of different species, absorption may take place with symptoms or even death, but these symptoms are those of an overdose of hypnotics, not those of chemical change secondary to liver damage, as in the case of carbon tetrachloride."

In adult doses ranging from 0.5 to 8 cc. the drug has been used on a broad scale and in some countries appears to have become the preferred anthelmintic for mass treatment of hookworm infection.[3] Although there is no way of obtaining any reliable figures on the matter, it is reasonable to believe that by now many hundreds of thousands of people have been treated with tetrachlorethylene.[4]

Because not a single death following the use of this drug has been reported in the literature thus far and because specific attention has not been called to untoward toxic symptoms, most textbooks on tropical medicine and parasitology and practically every physician experienced in the use of this drug with whom I have compared notes express the view that tetrachlorethylene is harmful only to the parasitic worms against which it is directed. Few are familiar with the case of Kendrick,[5] who, writing on the treatment of some 1,500 prisoners in the Madras penitentiary, recorded that 1 person showed signs of serious intoxication. About one hour after treatment this man complained of giddiness and soon thereafter completely lost consciousness; his pulse was barely perceptible, the eyelids were twitching and the whole body was covered with a cold, clammy perspiration. He slowly revived after two intramuscular injections of 1/32 grain (0.0018 Gm.) of strychnine and 1/50 grain (0.0012 Gm.) of digitalin; after the return of full consciousness no further symptoms developed. The man's personal history gave no clue as to the possible cause of this unexpected intoxication.

Recently Hare and Dutta,[6] working on a tea estate in India, reported favorably on the efficacy of 4 cc. doses of tetrachlorethylene as compared with 20 to 30 minims (1.2 to 1.8 cc.) of oil of chenopodium. With regard to toxicity, they stated that all their 84 patients experienced a sensation of drunkenness (which they rather enjoyed) lasting for an hour or so. A debilitated girl aged 18, suffered from severe vomiting, giddiness and heavy drowsiness. After cold had been applied to the head she recovered and was perfectly well by evening.

In a recent paper on the treatment of infection with the hookworm in India, Maplestone and Mukerji [7] wrote: "With regard to tetrachlorethylene we had our own experience of many years' use of the drug on human beings as well as our pharmacologic work on cats which showed that the dose of 4 cc. is so far below the dangerous limit that it is not necessary to reduce the dose in adults, however low their weight may be. In addition to our own experience, a good deal of other evidence of the safety of C_2Cl_4 has now accumulated and so far the only case reported of its apparent toxic effects is that of Kendrick (1929) in which the serious symptoms rapidly passed off. As it is now over ten years ago since this isolated case was reported and no similar ones have since been recorded, it seems reasonable to look on it as unique and of no real importance as an argument against the safety of tetrachlorethylene." In making the foregoing statement, Maplestone and Mukerji doubtless overlooked the details of a case recorded in America by Wright, Bozicevich and Gordon,[8] who in 1937 described the results of treating 50 boys for pinworms. One of their patients, a boy aged 11, who received a dose of only 1.1 cc. of tetrachlorethylene in 30 cc. of a saturated magnesium sulfate solution plus 60 cc. of water, showed symptoms of dizziness and depression one hour after treatment. The patient complained of eructations of the drug. One and a half hours after treatment he became cyanotic and during the next half hour lost consciousness four times. He was given 0.2 cc. of a 1:1,000 solution of epinephrine hydrochloride intramuscularly, after the administration of which his condition showed immediate improvement. This patient was subsequently found to have pulmonary tuberculosis.

During the course of the past twelve years I have accompanied several expeditions into various parts of the tropics of the New and the Old World where, because of helminthologic interest, anthelmintic treatment of several hundreds of natives of all ages and of several aboriginal races was carried out. Although other anthelmintics for intestinal worms, such as oil of chenopodium and carbon tetrachloride, were frequently used on these expeditions without incurring the slightest difficulty, the fear of an accident following carbon tetrachloride, with all the complications which a death might entail for an expedition far from civilization and hospital facilities, has led to a preference for tetrachlorethylene on account of its less sullied reputation. On four occasions I myself have received the drug in doses of 4 and 5 cc. Never has it produced more than a transient (and not unpleasant) sensation of levitation accompanied by a feeling of drowsiness that develops into a light sleep unless an effort is made to keep awake. Such apparently is the normal reaction to tetrachlorethylene. The soporific effects are evidence of absorption from the intestine, and the odor of the drug is detectable on the breath for several hours after medication.

It is my purpose in this paper to place on record 2 cases in which the effect of tetrachlorethylene was essentially the same

The observations on which this communication is based were made during the author's tenure of a John Simon Guggenheim Memorial Foundation Fellowship.

1. Hall, M. C., and Shillinger, J. E.: Tetrachlorethylene: A New Anthelmintic, Am. J. Trop. Med. **5**: 229 (May) 1925.

2. Lamson, P. D.; Robbins, B. H., and Ward, C. B.: The Pharmacology and Toxicology of Tetrachlorethylene, Am. J. Hyg. **9**: 430 (March) 1929.

3. Fernando, P. B.; D'Silva, M.; Stork, G. K. B., and Sinnatamby, G. R.: Tetrachlorethylene in the Treatment of Hookworm Disease, with Special Reference to Toxicity, Indian J. M. Research **26**: 759 (Jan.) 1939.

4. Lambert, S. M.: Hookworm Disease in the South Pacific: Ten Years of Tetrachlorides, J. A. M. A. **100**: 247 (Jan. 28) 1933. Faust, E. C.: The Pharmacopeia and the Physician: The Use of Anthelmintics, ibid. **108**: 386 (Jan. 30) 1937.

5. Kendrick, J. F.: The Treatment of Hookworm Disease with Tetrachlorethylene, Am. J. Trop. Med. **9**: 483 (Nov.) 1929.

6. Hare, K. P., and Dutta, S. C.: Comparative Value of Oil of Chenopodium and Tetrachlorethylene as Anthelmintics for Use in Mass Treatment, Indian M. Gaz. **74**: 198 (April) 1939.

7. Maplestone, P. A., and Mukerji, A. K.: Comparison of Thymol and Some Other Drugs in the Treatment of Hookworm Infection, Indian M. Gaz. **75**: 193 (April) 1940.

8. Wright, W. H.; Bozicevich, John, and Gordon, L. S.: Studies on Oxyuriasis: V. Therapy with Single Dose of Tetrachlorethylene, J. A. M. A. **109**: 570 (Aug. 21) 1937.

as that described in the solitary cases of Kendrick and of Wright, Bozicevitch and Gordon mentioned previously.

CASE 1.—A young Javanese man at the time of treatment was a schizophrenic patient in the psychopathic wards of the central hospital in Batavia. The man was in an advanced catatonic state, sitting or lying around apathetically and entirely incapable of making any cooperative effort. To cause the expulsion of some echinostome flukes with which he was infested, the man was given 4.5 cc. of medicinal tetrachlorethylene in water, and this dose was followed about thirty minutes later by 30 Gm. of magnesium sulfate in dilute aqueous solution. For about an hour the patient lay quietly in bed, but when approached later he was found in a comatose condition, all peripheral reflexes having been abolished. An intravenous injection of metrazol was without immediate effect, but the patient commenced to emerge from the coma about two hours later and exhibited no further symptoms of intoxication.

In attempting to find a cause for this disconcerting and totally unexpected reaction, suspicion was first cast on the purity of the drug. However, chemical analysis revealed no impurities such as phosgene. It was then inferred that the dose of tetrachlorethylene may have been too high in relation to the man's size and weight, the small Javanese natives as a race generally showing greater sensitiveness and requiring smaller therapeutic doses of most drugs than do Caucasians.

Holding that the reaction just described was an instance of deep anesthesia that presented no serious reason for abandoning the use of tetrachlorethylene, further treatments were carried out among the Javanese with doses ranging from 2 to 3 cc. without any untoward effects. On a later expedition into the hinterland of Celebes, a series of natives ranging in age from about 6 to 60 years were treated with doses ranging from 1 cc. to 4 cc., again without any undesirable effects. Not one of the recipients was sufficiently affected by tetrachlorethylene to discourage other members of the patient's family from requesting the medicine.

It was consequently a matter of great surprise and not a little consternation when, after an uneventful taking of 5 cc. of tetrachlorethylene by me to eliminate an experimentally induced infestation with flukes, a second member of the expedition fell into deep coma after taking a much smaller dose of the same drug a few days later.

CASE 2.—A healthy, well developed man, with nothing in his past history or present condition which would lead one to anticipate that the drug would not be well borne, was given a smaller quantity of the drug solely to determine its vermifugal efficacy on a quantitative basis. Three cc. of well emulsified tetrachlorethylene was taken with a quantity of water into an empty stomach.

While awaiting the lapse of half an hour before taking a saline purgative, he proceeded to make himself comfortable in an armchair and commenced to read. Ten minutes later he was seen to be breathing deeply as though in profound sleep. Attempts to awaken him were futile. The muscles were completely relaxed, most of the reflexes had disappeared, the pupils were somewhat constricted and the pulse remained full, strong and regular. This condition persisted for nearly two hours, at which time an intravenous injection of metrazol was given. To this injection there was immediate response, but although the subject regained partial consciousness it was several hours before the stupor had worn off completely. He recalled nothing after taking the drug, expressed his satisfaction at having had a restful sleep and proceeded to assist in washing the stools that he passed for the worms contained therein.

COMMENT

Both of these cases presented what appeared to be the action of a general anesthetic akin to ethylene or chloroform. They obviously indicate the need for hospitalizing or otherwise keeping under close surveillance all patients who are treated with tetrachlorethylene even in doses smaller than are usual. While for want of a better drug they should not discourage the use of tetrachlorethylene, they illustrate the truth of a remark which the late Dr. Maurice Hall made to me, to the effect that one cannot assume that any anthelmintic is entirely safe for human use until there are reliable reports on at least a million treatments without any untoward effects.

Special Article

GLANDULAR PHYSIOLOGY AND THERAPY

THYROID DYSFUNCTIONS AND THEIR TREATMENT

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This special article is published under the auspices of the Council on Pharmacy and Chemistry. It is one of a series which will be published in book form as the second edition of "Glandular Physiology and Therapy." The opinions expressed in this article are those of the author and do not necessarily represent the views of the Council.—ED.

CLASSIFICATION OF DISEASES [1]

A. HYPOFUNCTION
1. Primary
   (*a*) Cretinism
      (1) Sporadic
      (2) Endemic
   (*b*) Myxedema
      (1) Spontaneous
      (2) Postoperative
      (3) Postinfectious
      (4) During administration of iodine
2. Secondary
   (*a*) Hypopituitarism
   (b) Addison's disease

B. HYPERFUNCTION
1. Exophthalmic goiter (Symmetric toxic goiter)
2. Toxic adenoma (Nodular toxic goiter)
3. Mixed type

C. USUALLY NO DISORDER OF FUNCTION
1. Simple goiter (Symmetric nontoxic goiter, colloid goiter)
2. Nontoxic adenoma (Nodular nontoxic goiter)
3. Anomalies of development
   (*a*) Substernal goiter
   (*b*) Pyramidal lobe
   (*c*) Lingual goiter
   (*d*) Thyroglossal cyst
   (*e*) Lateral aberrant thyroid tissue
   (*f*) Thyroid tissue in teratoma
4. Thyroiditis
   (*a*) Suppurative: acute and chronic
   (*b*) Nonsuppurative: acute and chronic
   (*c*) Struma lymphomatosa
   (*d*) Riedel's struma
   (*e*) Chagas' disease (Trypanosoma cruzi)
5. New growths
   (*a*) Primary
      (1) Papillary adenocarcinoma—30 per cent
      (2) Carcinoma in adenoma (malignant adenoma)—38 per cent
      (3) Diffuse adenocarcinoma—31 per cent
      (4) Squamous epithelioma—1 per cent
      (5) Sarcoma—1 per cent
   (*b*) Secondary
      Metastases from other organs (rare)

ANATOMY AND PHYSIOLOGY

The chief object of this chapter is to discuss disorders of thyroid function. In order to do this intelligently, it is necessary to bear in mind a few pertinent

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1. Thompson, W. O.: Endocrinology, in Allen, E. van N.: Specialties in Medical Practice, New York, Thomas Nelson & Sons, 1940, vol. 2, chap. 9.

facts about the anatomy and physiology of the gland. The thyroid normally lies in the front of the neck just above the manubrium. In the normal adult it weighs about 25 to 40 Gm. According to the needs of the body, it supplies an internal secretion of which thyroxin is an integral amino acid. It appears to be capable of producing its hormone at the time of birth, and under normal circumstances its maximum weight is reached about the time of puberty. The gland contains numerous follicles, lined by epithelium and surrounded by a rich network of capillaries and lymphatics. The active secretion is stored in the colloid, to be supplied to the body according to demand. The height of the cells surrounding the acini is related to the amount of colloid which the latter contain, the cells being cuboid when the acini are distended with colloid and columnar when the acini contain little or no colloid. The maximum storage capacity of the gland for iodine is about 5 mg. per gram of dried gland, or a total of about 25 to 40 mg. for the normal gland.[2] Whenever the iodine content drops below 1 mg. per gram of dried gland hyperplasia appears.

The thyroid elaborates thyroxin, or its equivalent,[3] at the rate of about 0.3 mg. (0.2 mg. of iodine) per day,[4] which means that in the allotted three score years and ten the normal gland elaborates about 8 Gm. In the tissues outside the thyroid in a normal man there is the equivalent of about 10 to 14 mg. of racemic thyroxin.[5] These figures suggest that the iodine requirement of the normal thyroid is probably not more than 0.2 mg. per day and explain why so little iodine is required to prevent simple goiter and to produce a maximum reduction in basal metabolism in most patients with exophthalmic goiter (from 6 to 24 mg. daily). The maximum effect of thyroxin is dependent on the integrity of the molecule, and slight alterations greatly reduce, modify or abolish it.[6] In the interpretation of the presence or absence of hypothyroidism it is important to bear in mind that it takes about seventy to ninety days for the basal metabolism to drop from normal to its lowest level (— 40 to — 50 per cent) after omission of thyroid, and a still longer period for the full blown picture of myxedema to develop.

HYPOFUNCTION

Hypothyroidism may be primary or secondary. The primary type is caused by loss of functioning thyroid tissue, produced by operative removal, infection or primary atrophy of unknown cause. The gland is usually largely replaced by scar tissue. Raising the basal metabolism to normal results in a complete cure. The secondary type is caused by lack of adequate stimulation of the thyroid. The gland is commonly smaller than normal but may be normal in size or even greatly enlarged. The gland tends to be in a resting state and to show flat or low cuboidal epithelium with storage of colloid. Raising the basal metabolism to normal with desiccated thyroid may produce some improvement, but there is left a residue of symptoms, e. g., amenorrhea, which is not corrected by correcting the hypothyroidism. The primary type is seen in patients with cretinism or spontaneous myxedema and occasionally following subtotal thyroidectomy. The secondary type may occur in patients with hypofunction of the anterior lobe of the pituitary and in some patients with Addison's disease.

CRETINISM

Cretinism may be sporadic or endemic. Endemic cretinism is an end result of untreated endemic goiter lasting over a period of several generations. "Sporadic cretinism" is the term used to denote the cretinoid state that occasionally appears in the offspring of apparently healthy parents. In this country cretinism has been sporadic, but in Switzerland and some other mountainous areas it has been endemic. In this country endemic goiter has not lasted long enough in the goitrous areas to result in endemic cretinism. However, cretinism was endemic in many domestic animals in these areas before the diets of such animals were supplemented with iodine. Cretinism is simply myxedema of infancy. Added to the characteristic signs and symptoms of the disease are defects in the development of the skeleton and brain. There may be great disproportion between the two. In an older cretin the cerebration may be good and the development of the skeleton poor, or the reverse may be true. The skeleton can recover from a longer absence of thyroid secretion than the brain. The brain doubles in size during the first year of life by virtue of an increase in white matter, and an absence of thyroid function for only a few months results in permanent damage, the extent varying with the duration of the deficiency. On the other hand, a cretin may remain untreated until the age of 4 years and yet show growth of the skeleton to almost normal proportions. Differences in the susceptibility of the brain and skeleton to absence of thyroid function in the early years of life account for the marked discrepancies between mental and skeletal development observed in cretins.

It is obvious that early diagnosis is important, and yet it is difficult. At the time of birth the concentration of thyroxin in the child is normal if the concentration in the mother is normal. As previously shown, it then takes three months for the effects of absence of thyroid function to become evident. Determinations of metabolism in infants and young children are not satisfactory and are carried out in only a few clinics in this country. In most instances, before the diagnosis is made, irreparable damage has been done to the brain. Cretinism should be suspected at the first appearance of lethargy, constipation and failure to grow in length or to nurse properly. If treatment is instituted as soon as the signs and symptoms appear, almost completely normal development results. After the disease is well advanced, with appearance of the typical cretinoid facies, dry scaly skin and pot belly, the diagnosis is easy, but it is usually too late to make the child normal. Even then the diagnosis is often missed.

There is a great tendency to feed too large doses of thyroid, which produce nervousness, excessive perspiration and tachycardia and often lead to discontinuance of treatment for long periods. As a result, it is rare to see a cretin who has been treated continuously from the time the diagnosis was made. The dose of thyroid usually required varies from 1/10 grain

2. Marine, David, and Lenhart, C. H.: The Pathological Anatomy of the Human Thyroid Gland, Arch. Int. Med. **7**: 506 (April) 1911.
3. Salter, W. T.: The Endocrine Function of Iodine, Cambridge, Mass., Harvard University Press, 1940. Gutman, A. B.; Benedict, Ethel M.; Baxter, Blanch, and Palmer, W. W.: The Effect of Administration of Iodine on the Total Iodine, Inorganic Iodine, and Thyroxine Content of the Pathological Thyroid Gland, J. Biol. Chem. **97**: 303 (July) 1932.
4. Thompson, W. O.; Thompson, P. K.; Taylor, S. G., III; Nadler, S. B., and Dickie, L. F. N.: The Pharmacology of the Thyroid in Man, J. A. M. A. **104**: 972 (March 23) 1935.
5. Kendall, E. C.: Thyroxine, New York, Chemical Catalog Company, Inc., 1929. Thompson and others.[4]
6. Harington, C. R.: The Thyroid Gland: Its Chemistry and Physiology, New York, Oxford University Press, 1933. Thompson and others.[4]

(0.006 Gm.) of the U. S. P. material at 6 months to about 1 grain (0.064 Gm.) daily at the time of puberty. If the condition is not recognized for several years, the development of the brain may be so primitive that cerebral inhibition is lacking, and treatment may stimulate the patients so much that they may become very unruly. For this reason some cretins in institutions for the insane are untreated.

Prevention.—There is some evidence that animals with hypothyroidism are more liable to give birth to cretinous offspring than animals with normal thyroid function. It would therefore seem desirable to prevent conception in myxedematous women for several months after their thyroid function has been restored to normal and to watch their offspring carefully for the development of hypothyroidism. All women in goitrous areas should receive iodine throughout pregnancy.

MYXEDEMA

Myxedema denotes marked hypothyroidism in childhood and in adult life. It is more common in women than in men (4:1) and occurs most frequently during the fourth, fifth and sixth decades of life. The characteristic myxedematous appearance usually does not manifest itself until the metabolism drops to between —20 and —25 per cent. There are, however, a few striking exceptions to this rule. The cause is unknown in most instances, and the myxedema is spoken of as spontaneous. It may follow thyroidectomy, the spontaneous disappearance of exophthalmic goiter or an infection of the thyroid; in rare instances it may be produced by the preoperative or postoperative administration of iodine in patients with exophthalmic goiter. It is characterized by a slowing up of all reactions in the body, so that patients who have it become virtually hibernating. Outstanding among the manifestations are:

1. Puffiness of the face and eyelids, producing the typical myxedematous facies.
2. Swelling of the tongue and larynx, producing the typical hoarse, slow, slurred speech.
3. Dryness and roughness of the skin.
4. Falling out of hair all over the body, producing areas of alopecia (sometimes complete baldness), commonly almost complete absence of axillary and pubic hair, and sparseness and moth-eaten appearance of the eyebrows.
5. Poor memory, slowing of all mental reactions and dulness of the sensorium.
6. Constipation.
7. Reduction in basal metabolism.

In complete absence of thyroid function the basal metabolism drops to between —40 and —50 per cent, although all degrees of hypothyroidism are seen. All reactions that go on with a normal thyroid function also appear to go on in its absence, but at a slower rate. It takes between two and three months after the omission of treatment for the basal metabolism to drop to its lowest point, several more weeks or months for the characteristic myxedematous appearance to develop, and much longer for the changes in the skin and hair to reach their maximum. In some instances careful histories suggest that the disease may be present in early life in a form so mild it is not recognized and that under the stress and strain of living it gradually becomes more marked.

Too much emphasis has been placed on the supraclavicular pads of fat in the past. They are of no value in diagnosis. The thyroid hormone does not exercise a specific influence on fat metabolism, and hypothyroidism is not to be regarded as a cause of obesity. The increased weight is caused largely by deposition of water, and patients rarely lose more than 20 pounds (9 Kg.) during treatment. The weight lost consists mostly of water containing nitrogen and electrolytes. Boothby and co-workers[7] showed that the edema of myxedema is an albuminous deposit with about the composition of egg white.

Changes in the Blood.—In patients with myxedema any or all of the following changes may be present in the blood:

1. Secondary anemia, which is sometimes accompanied by eosinophilia and basophilia.
2. A decrease in the total quantity of circulating plasma.
3. An increase in the concentration of protein in the plasma.
4. A corresponding decrease in the concentration of water in the plasma.
5. A decrease in the concentration of chloride in the plasma and a corresponding increase in the concentration of bicarbonate, the total base usually remaining constant.
6. An increase in the concentration of cholesterol in the plasma.[8]

Changes in the Circulation.—The following changes are noted in the circulation:

1. A marked decrease in the minute volume of the heart and a prolongation of the circulation time. The opposite changes are noted in hyperthyroidism. These changes are associated with alterations in the mechanical work required of the heart and may represent adaptations of the circulation to variations in the demand for oxygen.
2. Myxedematous changes in the heart muscle, interfering with its efficiency. The transverse diameter of the heart is often increased, the sounds become weak, the pulse pressure drops, all of the complexes in the electrocardiogram are reduced in amplitude, and the T waves in leads 1, 2 or 3 may be inverted. The change in the heart muscle may so interfere with cardiac efficiency that decompensation develops, with characteristic pitting edema of dependent portions of the body (so-called myxedema heart). The decompensation and edema in this condition do not clear up with digitalis but promptly disappear with thyroid.

Difference Between Myxedema and Cardiac Edema.—In myxedema there is general increase in intracellular water. When pitting develops it usually is the result of superimposed cardiac edema. In cardiac edema there is marked increase in intercellular water, chiefly in dependent portions of the body. It is not associated with the increased deposition of protein seen in patients with myxedema.

Changes in the Cerebrospinal Fluid.—In myxedema there is usually a well marked increase in the concentration of protein in the cerebrospinal fluid, while the opposite change is observed with toxic goiter.[9] Values as high as 300 mg. per hundred cubic centimeters have been observed in cases of myxedema, compared with the normal of 25 to 40 mg. per hundred cubic centi-

7. Boothby, W. M.; Sandiford, I.; Sandiford, K., and Slosse, J.: The Effect of Thyroxin on the Respiratory and Nitrogenous Metabolism of Normal and Myxedematous Subjects: I. A Method of Studying the Reserve or Deposit Protein with a Preliminary Report of the Results Obtained, Tr. A. Am. Physicians **40**: 195, 1925.

8. Hurxthal, L. M.: Blood Cholesterol in Thyroid Disease: II. Effect of Treatment, Arch. Int. Med. **52**: 86 (July) 1933.

9. Thompson, W. O.; Thompson, P. K.; Silveus, E., and Dailey, M. E.: The Protein Content of the Cerebrospinal Fluid in Myxedema. J. Clin. Investigation **6**: 251 (Oct.) 1928.

meters. No other significant change has been noted in the fluid. The high concentration of protein in the cerebrospinal fluid, like that of the cholesterol in the blood, is sometimes of diagnostic value, especially in regard to cretins, although the values for both vary too much for purposes of routine diagnosis. The cerebrospinal fluid findings in myxedema resemble those in some cases of brain tumor and are similar to those in diabetes mellitus.

Changes in Calcium Metabolism.—In hypothyroidism the urinary excretion of calcium is diminished, and the bones sometimes show an increase in density, whereas in hyperthyroidism the opposite changes are noted.[10] In rare instances the decalcification of the skeleton in toxic goiter is so marked that spontaneous fractures occur. These alterations in the metabolism of calcium in thyroid disease occur without corresponding changes in the concentration of calcium in the serum, in contrast to the changes in hypoparathyroidism and hyperparathyroidism.

Sexual Changes.—There is commonly decrease in libido, decrease in axillary and pubic hair and often sterility. The menstrual history is variable. The flow may be excessive, simulating incomplete abortion; there may be scantiness of menstruation with prolongation of the intermenstrual period, or there may be complete absence of menstruation. In hyperthyroidism there is often scantiness of menstruation with or without prolongation of the intermenstrual periods.

Pathologic Anatomy.—The gland is usually largely replaced by scar tissue. In some instances, however, a goiter is actually present, suggesting either inadequate stimulation of the thyroid or enlargement of a diseased gland in an attempt to supply an adequate amount of secretion. The gland in such a patient may enlarge during the period of myxedema and decrease in size when thyroid is administered. There is some separation of the fibers of skeletal and cardiac muscles and of the cells of the skin by the myxedematous condition.

Differential Diagnosis.—Myxedema may be confused with chronic nephritis, Simmonds's disease and pernicious anemia. In both myxedema and chronic nephritis there may be secondary anemia, hypertension and some albuminuria. However, the typical myxedematous appearance is absent in patients with chronic nephritis. In nephrosis the basal metabolism may be as low as in myxedema, but the marked general pitting edema, the reduction in the concentration of protein in the serum, the reversal of the albumin-globulin ratio, the marked albuminuria and the absence of the myxedematous facies make it comparatively easy to distinguish the two diseases. In Simmonds's disease there may be marked lowering of the basal metabolism and amenorrhea, but the cachexia and the absence of the myxedematous appearance and of roughness and dryness of the skin usually make it possible to exclude myxedema. In pernicious anemia the lemon yellow tint of the skin, the characteristic blood findings and the absence of the myxedematous facies readily make it possible to exclude myxedema. In rare instances the two diseases coexist, and then appropriate treatment must be given for each.

As the use of basal metabolism apparatus becomes more widespread, there is a tendency for hypothyroidism to be detected in its early stages more commonly than before. However, the diagnosis of myxedema is still often not made until the disease is well advanced and then only when the patient visits a special clinic. Alterations in the basal metabolism must be correlated with the clinical picture. There are patients with basal metabolism of — 20 to — 25 per cent who do not appear myxedematous and who are not improved by the administration of thyroid. The cause of the low basal metabolism in them is obscure.

In Addison's disease there is often moderate depression of the basal metabolism, and in rare instances myxedema is present. Patients are often improved by the administration of thyroid, but it is not known at present whether the adrenal cortex affects the thyroid directly or indirectly.

TREATMENT OF PRIMARY HYPOTHYROIDISM

The following directions and considerations are important in the management of the primary type of hypothyroidism:

1. Administer the minimum amount of desiccated thyroid necessary to maintain a normal level of metabolism. The average dose required for maintenance in thyroidless adults is from 1½ to 2 grains (0.096 to 0.128 Gm.) of thyroid U. S. P. (0.18 to 0.23 per cent iodine) daily. In cretins, as previously stated, the dose varies from ⅒ grain at the age of 6 months to 1 grain daily at the age of puberty.

2. Begin with an inadequate dose (1 grain daily in most adults under 40 years of age) and increase the amount gradually after several weeks until the correct amount is being administered.

3. Avoid a large initial dose in all cases, particularly if the patient shows arteriosclerosis and coronary disease, because of the danger of precipitating coronary thrombosis. For such a patient the initial dose should not exceed ½ grain (0.032 Gm.) daily. If angina develops during treatment, the metabolism should be adjusted at a somewhat subnormal level. Besides coronary accidents, the administration of large initial doses of desiccated thyroid or of thyroxin, as advocated in some clinics, may produce symptoms of thyroid intoxication, including aching and marked tenderness of muscles, sometimes a fever (as high as 104 F.), occasionally nausea and rarely vomiting. By raising the metabolism slowly, these unpleasant symptoms are avoided and the danger of accidents is greatly minimized.

4. Make changes in the dose slowly, because of the slow adjustment. At least two months is required for complete adjustment to any dose.

5. In recording the dose of thyroid always state the iodine content.

6. Do not expect thyroxin to revive untreated patients after they have become almost moribund; the action of the drug is too slow. Such an emergency should be prevented by early treatment.

7. Do not administer thyroxin intravenously except in the rare instances in which there is a question whether or not the patient is taking the dose of thyroid prescribed. Thyroxin works well when given in alkaline solution by mouth but possesses no advantage over desiccated thyroid.

When secondary anemia is present, it is usually not corrected by the administration of thyroid alone but requires in addition the administration of large doses of iron.

Extravagant claims are made for various preparations of thyroid from which the toxic material is supposed to have been removed. In my experience these claims

10. Aub, J. C.; Bauer, Walter; Heath, Clark, and Ropes, Marion: Studies of Calcium and Phosphorus Metabolism: III. The Effects of the Thyroid Hormone and Thyroid Disease, J. Clin. Investigation **7**: 97 (April) 1929.

have appeared to be without foundation: such preparations have possessed no advantage over desiccated thyroid. As a matter of fact, all of the symptoms of intoxication associated with the administration of large doses of desiccated thyroid have been associated also with the administration of the pure substance, thyroxin.

TREATMENT OF SECONDARY HYPOTHYROIDISM

The treatment of secondary hypothyroidism is also best carried out at present by the administration of thyroid, although this represents only part of the treatment. In the patient with hypopituitarism the thyroid may be stimulated by administering the thyrotropic factor of the pituitary, but, apparently because of development of immunity, the effect lasts only a few weeks even though the treatment is continued. Some improvement in the stimulation type of treatment may be expected with improvement in anterior pituitary extracts.

LOW BASAL METABOLISM WITHOUT MYXEDEMA

Reference has already been made to a group of patients with low basal metabolism in whom the administration of thyroid does not produce improvement. In the interpretation of the low rates in such patients it may be pointed out that the total metabolism may be altered in a variety of ways which do not involve any change in thyroid function. The increases effected by epinephrine, muscular exercise, dinitrophenol, dinitroorthocresol and diiodothyronine occur too quickly to be the result of any change in thyroid function. In a patient with myxedema the metabolism may be raised to normal with dinitrophenol or dinitroorthocresol without any change in the myxedematous condition.[4] The possibility must therefore be entertained that some unknown factor or factors outside the thyroid may directly affect oxidation. In some persons normal thyroid function may be present in spite of basal metabolism 20 to 25 per cent below normal. In such persons a normal level of metabolism would represent a thyrotoxic one. These considerations may explain occasional instances in which clinical relief from thyrotoxicosis appears to have been associated with a reduction of the basal metabolism from a standard normal to a low level. However, the greatest caution must be exercised in the interpretation of all such apparent instances of improvement if needless thyroidectomy is to be avoided.

Unless the basal metabolism is depressed more than 25 per cent below normal, myxedema is usually not present and the symptoms are indefinite, making it difficult to tell by the clinical picture alone whether or not hypothyroidism is present. A therapeutic test with thyroid must therefore be made. Hypothyroidism of either the primary or the secondary type may be considered to exist in a patient with low basal metabolism when clinical improvement is produced by raising the basal metabolism to normal. When no improvement occurs, it may be concluded that hypothyroidism is not present and that the administration of thyroid is futile.

TOXIC GOITER

There is some question as to whether or not there are two types of toxic goiter. Plummer[11] attempted to differentiate two types (exophthalmic goiter and toxic adenoma) on the basis of function. According to his hypothesis, there is with toxic adenoma simple hyperthyroidism, whereas with exophthalmic goiter there is simple hyperthyroidism plus production of an abnormal product. This abnormal product, which he thought might be a deficiently iodinized thyroxin, accounted for the peculiar emotional instability with exophthalmic goiter, which distinguished it from toxic adenoma. Up to the present time, observations on the calorigenic and clinical effects of compounds closely related to thyroxin (notably thyronine and diiodothyronine) have not supported Plummer's hypothesis. There do, however, appear to be certain differences between the two diseases. In the patient with exophthalmic goiter the goiter and the thyrotoxic symptoms usually appear abruptly at about the same time, whereas in the patient with toxic adenoma the thyrotoxic symptoms commonly appear insidiously after goiter has been present for several years (fourteen and a half years on the average).[12] In general, emotional instability is more marked in patients with symmetrically enlarged goiters than in patients with nodular goiters.

The terms used to denote the types of toxic goiter are misnomers. This is particularly true of the syndrome described as exophthalmic goiter, which may be present in a patient without a goiter and without exophthalmos. However, even though the thyroid is not enlarged, it is usually firmer than normal. To produce descriptive terms that are more accurate, the American Association for the Study of Goiter has proposed that "symmetric toxic goiter" and "nodular toxic goiter" be substituted for "exophthalmic goiter" and "toxic adenoma," respectively. Similarly, they have suggested that simple goiter and nontoxic adenoma be called "symmetric nontoxic goiter" and "nodular nontoxic goiter," respectively.

Cause.—The cause of toxic goiter is not known. Among the most plausible possibilities are overproduction of the thyrotropic factor by the anterior lobe of the pituitary, some disorder of the sympathetic nervous system, a disturbance of some center controlling thyroid function in the base of the brain and some abnormality inherent in the thyroid itself. Great attention has been focused in recent years on the interrelations of the thyroid and the pituitary.[13] It is definitely established that integrity of thyroid function is dependent on integrity of pituitary function and that hypothyroidism and hyperthyroidism may be secondary to corresponding states in the anterior lobe of the pituitary, e. g., chromophobe adenoma and acromegaly, respectively. In acromegaly the basal metabolism may show a reduction during the administration of iodine just as in exophthalmic goiter. In patients with normal or slightly depressed basal metabolism all of the symptoms of toxic goiter except exophthalmos may be produced by administration of an anterior pituitary extract containing the thyrotropic factor.[14] The severity of toxic goiter may be increased in the same manner. The thyrotropic factor is inert in the absence of thyroid tissue capable of function. However, in spite of all these convincing observations, there is so far no positive proof that the pituitary is concerned in the clinical disorder of toxic goiter.

Incidence with Regard to Age and Sex.—Exophthalmic goiter occurs most frequently in persons between

11. Plummer, H. S.: The Clinical and Pathologic Relationships of Hyperplastic and Non-Hyperplastic Goiter, J. A. M. A. **61**: 650 (Aug. 30) 1913.

12. Haines, S. F.: Adenomatous Goiter with Hyperthyroidism, Tr. Third Internat. Goiter Conf. & Am. A. Study Goiter, 1938, p. 198.

13. Collip, J. B.: Inhibitory Hormones and Principle of Inverse Response, Ann. Int. Med. **8**: 10 (July) 1934. Uhlenhuth, E.: Thyreoactivator Hormone: Its Isolation from Anterior Lobe of Bovine Pituitary Gland and Its Effects on Thyroid Gland, Tr. Am. A. Study Goiter, 1936, p. 25.

14. Thompson, W. O.; Thompson, P. K.; Taylor, S. G., III, and Dickie, L. F. N.: The Influence of the Pituitary in Thyroid Disease, West. J. Surg. **47**: 4 (Jan.) 1939.

the ages of 15 and 50.[15] Both types of toxic goiter are more common in women than in men, in the proportion of 4 or 5 to 1. The sex ratio varies from place to place and from time to time and to some extent with age, the difference in incidence in the two sexes being less marked in the very young and the very old. The cause for the greater frequency of the disease in women is unknown.

Pathologic Anatomy.—In exophthalmic goiter the gland is characterized by papillary projections into the acini, decrease in the amount of colloid and in the iodine content and often by increase in the lymphoid tissue between the follicles. These changes are associated with increase in the concentration of iodine in the blood and increase in the excretion of iodine in the urine.[16] In some instances thick bands of fibrous tissue are observed throughout the gland, and the capsule may be adherent to surrounding tissues. Often there is proliferation of lymphoid tissue throughout the body, together with persistence of the thymus. According to Warthin, certain persons are born with this so-called thymicolymphatic, or Graves' constitution and are predisposed to the development of toxic goiter. Relative lymphocytosis in the blood has been described and much was made of it by Kocher. When iodine is administered, the papillary projections decrease or disappear, the colloid and iodine content of the gland increase, and the organic iodine content of the blood decreases. These changes are usually associated with decrease in the basal metabolism. The mechanism of the action of iodine is unknown. In a few instances the response to iodine may be reversible, the administration of inadequate doses being associated with increase in basal metabolism and the administration of adequate doses immediately afterward with decrease.[17] The minimum dose of iodine that would produce any effect in most patients in Boston was about 0.75 mg. per day, and the minimum dose that would produce a maximum effect was about 6.0 mg. per day. For some patients a larger dose is required to produce a maximum effect. In Chicago as much as 24.0 mg. per day has been necessary in some patients.

It has been pointed out by Marine[2] that the histologic structure of the thyroid and its response to iodine are the same in simple goiter and in exophthalmic goiter. In the individual nodules of glands with toxic adenoma the same changes may be observed as are seen in glands with exophthalmic goiter, but they are not so characteristic. In toxic adenoma the goiter is commonly of long standing, and various degenerative changes are seen, including thick bands of scar tissue, colloid degeneration, hemorrhage and formation of cartilage and bone.

Signs and Symptoms.—The more common signs and symptoms of toxic goiter are:

1. Goiter (absent in rare instances, although the gland is always firmer than the normal)
2. Nervousness
3. Tremor
4. Tachycardia
5. Palpitation
6. Dyspnea
7. Loss of weight
8. Increase in basal metabolism
9. Exophthalmos (in about from 60 to 70 per cent of patients with exophthalmic goiter)
10. Various other ocular signs, the most important being puffiness of the eyelids, lid lag (von Gräfe) and poor convergence (Möbius)
11. Systolic thrill and bruit, usually most marked over the superior poles (not present in adenomatous goiter)
12. Emotional instability
13. Muscle weakness
14. Early fatigue
15. Increased perspiration
16. Diarrhea (in about one third of the cases, usually the more severe ones)
17. Pressure symptoms (one quarter of the cases)
18. Nausea and vomiting (rare and unfavorable signs)

Crisis.—Sometimes in either the treated or the untreated disease a condition known as a crisis develops. A crisis is characterized by loss of appetite, nausea, vomiting, gradually increasing heart rate, marked weakness, loss of weight and sometimes by diarrhea and fever. If no treatment has previously been given, a crisis can often be controlled by administration of iodine, but this condition may appear during treatment or fail to respond to all known therapeutic measures and result in the death of the patient before operative procedures can be carried out. A crisis may develop during the postoperative period and under these circumstances usually indicates inadequate preoperative preparation. In a crisis the cause of the disease is presumably acting with great intensity.

Differential Diagnosis.—Toxic goiter may have to be distinguished from nontoxic goiter, neurocirculatory asthenia, emotional disturbances from other causes, acromegaly and pulmonary tuberculosis. In nontoxic goiter, neurocirculatory asthenia and emotional disturbances from causes other than thyrotoxicosis, the basal metabolism is normal. In the patient with simple goiter the thyroid gland is softer than that of the patient with toxic goiter, and a bruit is usually not heard. In acromegaly there may be a goiter, high basal metabolism and exophthalmos, but the characteristic skeletal changes readily make it possible to distinguish the two diseases. The roentgenologic findings, fever and poor appetite readily distinguish pulmonary tuberculosis, which does not very often present a problem in diagnosis. In the leukemias and polycythemia vera the metabolism may be elevated, but these diseases rarely present problems in diagnosis.

Whenever there is any doubt about the diagnosis, it is important to determine (1) the level of the basal metabolism and (2) the effect of administration of iodine on this level.

Treatment.—There are three ways of treating toxic goiter: (1) by subtotal resection of the gland after suitable preparation of the patient, (2) by roentgen irradiation of the gland and (3) medically (chiefly by iodine and rest).

It is generally agreed that subtotal resection of the gland after suitable preparation of the patient represents the best method of treatment.[18] Treatment, therefore, involves an intelligent combination of surgical and medical measures. Roentgen ray therapy is valu-

15. Means, J. H.: The Thyroid and Its Diseases, Philadelphia, J. B. Lippincott Company, 1937.
16. Curtis, G. M., and Puppel, I. D.: The Iodine Metabolism in Thyroid Disease, Tr. Third Internat. Goiter Conf. & Am. A. Study Goiter, 1938, p. 367.
17. Thompson, W. O.; Thompson, P. K., and Cohen, A. C.: The Range of Effective Iodine Dosage in Exophthalmic Goiter: IV. The Effect on Basal Metabolism of the Daily Administration of About 0.75 Mg. of Iodine, Arch. Int. Med. **49**: 199 (Feb.) 1932.
18. Lahey, F. H.: Surgery in Hyperthyroidism, Tr. Third Internat. Goiter Conf. & Am. A. Study Goiter, 1938, p. 297.

able in a few selected cases in which operation is contraindicated, but its results are too delayed and too uncertain to make it practical in most instances. In a few cases in which the symptoms are mild the disease may be held in check by iodine alone until it disappears, but this form of treatment must be carried out with the greatest care because the disease is characterized by remissions and relapses and a mild form of the disease may at any time become a severe one.

The outcome of operation is determined by the condition of the patient at the time of operation and by the skill of the surgeon. Both factors are important, but our data indicate that the condition of the patient is the more important.[19] The operation is an elective one and should be carried out only when the condition of the patient justifies this. As already pointed out, postoperative crises usually mean inadequate preoperative preparation. Thyroidectomy is never an emergency operation and when done as such commonly results in the death of the patient. With some patients it may be necessary to take several months for adequate preparation. The preoperative management should be carried out in the medical service of a hospital by a specially trained internist. The internist should continue his observation of the patient in the immediate postoperative period as well as later, because many of the problems that arise are medical in nature.

The following points are important in preparing patients for operation:

1. The diet administered should be sufficiently high in calories to produce a gain in weight (usually 4,000 to 5,000 calories daily).

2. The condition of the patient must be improved by the administration of iodine. Within wide limits the size of the dose and the form in which it is administered are not important. For routine purposes it is desirable to administer 5 minims (0.3 cc.) of compound solution of iodine or 1 grain (0.06 Gm.) of sodium or potassium iodide three times a day. It used to be thought that operative procedures should be carried out as soon as the basal metabolism showed its maximum reduction during the administration of iodine, because of the danger of a serious exacerbation of the disease with continued administration. The danger of this occurrence has been greatly exaggerated, and it is well established that maximum clinical improvement from iodine does not necessarily coincide with maximum reduction in basal metabolism. My associates and I rarely recommend operative procedures until about one week has elapsed after the time of maximum reduction in basal metabolism and do not hesitate to delay operation as long as is necessary to improve the condition of the patient.

3. Rest is very important, but patients must not be confined to bed. Some activity should be allowed and encouraged in order to preserve muscle tone, except in the presence of a crisis or of cardiac decompensation. Patients should be prepared in the hospital, away from the stress and strain of the home environment.

4. Roentgen ray treatment should be considered for patients with high metabolic rates refractory to iodine.

5. Patients with cardiac decompensation should be conditioned for operation by the administration of digitalis.

It is usually unwise to operate when:

1. The patient fails to gain or is losing weight.

2. Emotional instability and muscle weakness are pronounced.

3. The basal metabolism is plus 60 per cent or higher in spite of the administration of iodine.

4. The disease is increasing rapidly in severity.

5. Less than two weeks has elapsed since an infection of the upper respiratory tract cleared up.

6. Cardiac decompensation is present.

Each patient presents an individual problem, and there are, of course, exceptions to these rules. For example, often, if a patient is gaining weight steadily, we do not hesitate to operate even though the basal metabolism remains 60 or 70 per cent above normal in spite of the administration of iodine. Gain in weight is the single most important sign in gaging the risk of operation. With it there are usually a reduction in emotional instability and an increase in strength. Whenever there is any doubt, it is best to err on the side of conservatism. Operation can always be delayed, but after a postoperative crisis has set in, often nothing will stop it. Unless cardiac decompensation is present, the criteria of operability are the same in the presence of organic heart disease as in its absence.

When the patient cannot be prepared properly by the procedures outlined, sufficient improvement to justify the carrying out of operative procedures may be produced by roentgen ray treatment of the thyroid (eight to twelve treatments given at weekly intervals).

Immediate Preoperative Preparation.—It is important:

1. To make a careful search for an infection of the upper respiratory tract just before the patient goes to the operating room.

2. To administer a carbohydrate meal from six to eight hours before operation, to prevent the development of acidosis in the postoperative period.

3. To administer the regular dose of iodine with this meal.

4. To institute, twenty-four hours before the scheduled time of operation, some program suitable for the control of emergencies when the disease is complicated by diabetes.

Immediate Postoperative Treatment.—It is important:

1. To observe the wound carefully for early detection of excessive bleeding.

2. To observe the patient carefully to detect respiratory difficulty as soon as it arises, either from laryngeal or from tracheal obstruction. When only one vocal cord is paralyzed, serious respiratory difficulty usually does not develop.

3. To secure the services, for the first forty-eight hours, of a specially trained nurse who will report trouble as soon as it arises.

4. To have available facilities for emergency passage of a life-saving tube and performance of a tracheotomy. A tracheotomy is rarely necessary, but when it is necessary it usually has to be done in a hurry.

5. To administer intravenously a suitable combination of salt and dextrose for prolonged or excessive vomiting, a thyroid crisis or a circulatory collapse (1 liter of 5 per cent dextrose in physiologic solution of sodium chloride every six hours).

6. To administer iodine until the patient's discharge from the hospital, to control any residual thyrotoxicosis.

19. Thompson, W. O.; Taylor S. G., III; Meyer, K. A., and McNealy, R. W.: Experiences in Treating Toxic Goiter in a Large Public Hospital, Ann. Int. Med. **12**: 217 (Aug.) 1938.

7. To search for parathyroid tetany on the second to the fourth postoperative day and, if observed, to control it with suitable measures.

In most instances it is desirable to allow patients out of bed within twenty-four to forty-eight hours after thyroidectomy, to prevent their becoming bedridden and to shorten their postoperative course.

Deaths.—By the application of the principles outlined, my associates and I[19] were able to reduce the operative mortality at the Cook County Hospital during the period from 1932 to 1937 from 10.8 to 1.6 per cent. About 40 per cent of the deaths in our series were caused by sudden respiratory difficulty, about 30 per cent by pneumonia and about 20 per cent by crises. However, after 1934 there was not a single death from a crisis, a fact which we attribute to more adequate preoperative preparation of the patients. The deaths from sudden respiratory difficulty were usually associated with bilateral paralysis of the vocal cords with or without pressure on the recurrent laryngeal nerves from hard blood clots under the strap muscles, and in one instance death was caused by pressure from a hematoma on a collapsible trachea. Preoperative infections of the upper respiratory tract appear to play an important role in the development of postoperative pneumonia.

Results of Treatment.—Following subtotal thyroidectomy the basal metabolism in about 70 per cent of cases drops to normal in from ten to fourteen days and remains normal for the rest of the patient's life. In about 20 to 25 per cent of cases it finally drops to a subnormal level, although the development of complete myxedema is rare. In about 5 to 10 per cent of cases the disease persists or recurs. A true recurrence is rare; in most cases postoperative thyrotoxicosis represents persistence of the disease.

Most patients showing low basal metabolism are improved by the administration of thyroid. The treatment of the persistent or recurrent disease is the same as that of the untreated disease, unless some complication, such as paralysis of a vocal cord, makes it undesirable to carry out further operative procedures. Two points are important in determining whether or not the disease has been eliminated by operation:

1. A basal metabolic rate of plus 15 per cent or higher during the administration of iodine from ten to fourteen days after operation usually means that the disease has not been abolished. On the other hand, if the basal metabolism is normal from ten to fourteen days after operation and iodine is being administered, it is uncertain whether the disease is still present or not.

2. If the basal metabolism remains within normal limits for as long as two months without the administration of iodine, a cure can almost be assured.

SIMPLE GOITER

In simple goiter there is symmetric enlargement of the thyroid, usually associated with no disturbance of function, although in some instances there is mild hypothyroidism. Like most thyroid diseases, it is more common in women than in men and is more common during periods of increased stress on the thyroid, namely, at puberty and during pregnancy. As the incidence in the population increases, the ratio of male to female patients increases. The response of simple goiter and exophthalmic goiter is the same histologically to administration and withdrawal of iodine, but the causes of the two diseases are entirely different. Simple goiter is not commonly a precursor of exophthalmic goiter. The cause of exophthalmic goiter is unknown. The most important cause of simple goiter is a deficiency of iodine. Other factors are involved in this type of goiter. Its production in a variety of ways and the greater susceptibility of some persons as demonstrated by its tendency to occur in families are consistent with this point of view. However, most of the causes appear to act by rendering iodine unavailable to the thyroid. Iodine is very effective in the prevention of simple goiter, and there is a close parallelism between the iodine content of the soil and the incidence of simple goiter in various parts of the world.[20] The incidence has been high in the Himalayan Mountain regions of South Central Asia; the Alpine, Pyrenean and Carpathian Mountain regions of Europe; the Andean Plateau and Southeastern Brazil in South America; while in North America its incidence has been high in the St. Lawrence River Basin and Great Lakes district, the Dakotas and adjacent Canadian provinces, and the Pacific Northwest including Oregon, Washington and British Columbia.

Pathologic Anatomy.—The histologic picture of the gland depends largely on the duration of the iodine deficiency. When the gland is subjected to an adequate supply of iodine, it first uses up the iodine it has stored in its own colloid. Marine and Lenhart[2] have shown that when the iodine content of the gland drops below 1 mg. per gram of dried gland, papillary projections into the acini appear, and the epithelium begins to change from columnar to cuboidal. The extent of these changes depends on the degree of depletion of colloid. A similar quantitative relationship is observed in patients with exophthalmic goiter. According to Marine and Lenhart,[2] the gland increases in size in a steplike fashion. After a period of hyperplasia, the subject may receive a supply of iodine, whereupon the gland stores colloid, the papillary projections disappear, the epithelium reverts to cuboidal form and the gland is in a resting or involutional stage. Then again come a deficiency and an abundance of iodine, and the cycle is repeated. These pathologic considerations readily explain why in the treatment of simple goiter the gland usually does not decrease in size. In fact, at first it may increase in size and then remain stationary. Prevention of further increase in size is all that can be promised from treatment. However, in rare instances a marked regression in size does occur under the influence of iodine. Another type of change may occur. Groups of acini may become much more distended with colloid than surrounding acini, which become compressed and disintegrate and are replaced by scar tissue forming a nodule surrounded by a capsule. Wegelin and Rienhoff have suggested that many nodules appear in this way, and it would seem that the development of adenomatous goiter is commonly an end result of simple goiter.

Treatment.—An effort should be made to cause a reduction in size by first giving a large excess of iodine (5 minims of compound solution of iodine or 1 grain of potassium iodide or sodium iodide daily) for two or three months. If no reduction in size occurs, a much smaller dose should be administered, such as the amount in iodized salt or 1 minim (0.06 cc.) of compound solution of iodine once a week. If there is associated hypothyroidism, a marked decrease in the size of the goiter may occur during the administration of desiccated thyroid.

20. McClendon, J. F.: Iodine and the Incidence of Goiter, New York, Oxford University Press, 1939.

Instead of giving iodine in small daily doses, Marine and Kimball [21] have shown that it is possible to prevent simple goiter by giving an excess of iodine for two or three weeks twice a year. The explanation for this is simple. The storage capacity of the thyroid for iodine is about 5 mg. per gram of dried gland, or a total of about 25 mg. for the average normal thyroid. If all of this iodine were available for the production of thyroxin, it would yield 37.5 mg. of thyroxin, which is enough to maintain normal thyroid function for one hundred and fourteen days. On the same basis, a second period of excess of iodine would result in the formation of a normal supply of the thyroid hormone for a total of two hundred and twenty-eight days. The additional iodine in the food and water would in most instances be adequate for maintaining normal thyroid function throughout the year.

Prophylaxis.—It is more important to prevent simple goiter than to treat it after it has developed. This is best done by the universal use of iodine in goitrous areas, preferably in the form of iodized salt. It has been previously pointed out that the iodine requirement of the normal thyroid probably does not exceed 0.2 mg. daily. The iodized salt used in this country contains about 200 mg. of iodine per kilogram (0.02 per cent), which would mean that a person who takes 5 Gm. of salt daily would get 1 mg. of iodine. This amount may be greater than is necessary. The iodized salt used in Switzerland contains only one fortieth of this amount and yet has proved effective except at puberty and during pregnancy. Marine has advocated the use of salt containing 10 mg. of iodine per kilogram, one twentieth of the amount now being used. More work needs to be done in this country on the prophylactic value of doses of iodine smaller than are now being used.

Importance of Prophylaxis.—Goiter presents a problem on every continent and affects not only man but also domestic animals. The prevention of simple goiter means the elimination of endemic cretinism, which in the past has caused great economic loss in both man and domestic animals. Its prevention also means a great reduction in the incidence of nontoxic adenoma and therefore presumably of toxic adenoma and of carcinoma. It therefore represents a public health problem of the first magnitude in many parts of the world.

NONTOXIC ADENOMA (NODULAR NONTOXIC GOITER)

Adenoma of the thyroid may develop at any point from the base of the tongue to the diaphragm. The growths vary in size from microscopic nodules to nodules many centimeters in diameter, are commonly multiple and, as a rule, lie in the usual location of the thyroid. Some substernal extension is common. Occasionally the whole adenomatous goiter lies in the mediastinum, and rarely a substernal nodule is encountered with the remainder of the thyroid in the usual location.

The diagnosis rarely presents any problem except when the goiter is confined to the substernal space or when thyroid nodules are confused with parathyroid nodules.

Pathologic Anatomy.—The most common type of adenoma is that arising in simple goiter. In this type of goiter the hyperplastic and colloid phases (colloid adenoma) of simple goiter are encountered. Various types of degenerative changes may be observed in goiters of long standing. Several acini may become greatly distended with colloid; their walls may rupture and coalesce, giving rise to large gelatinous masses. Thick bands of scar tissue, hemorrhage and formation of cartilage and bone are also noted.

Nodules may arise from fetal rests. These are of two types. One contains columns of cells (embryonic adenoma) and the other small, closely packed acini (fetal adenoma). It has been suggested that the more undifferentiated the type of cell in an adenoma the more malignant the carcinoma arising from it.

Treatment.—Routine removal of all nodules of the thyroid has been suggested in some quarters in order to prevent development of carcinoma and prevent toxic adenoma. Among persons past the age of 45, thyrotoxicosis develops in about 1 in 4 and carcinoma in about 1 in 200. If all nodules were routinely removed, the mortality, except in leading centers, would probably be higher than the mortality from carcinoma. The incidence of tetany (less than 1 per cent) and of paralysis of the vocal cords (perhaps 5 per cent) must also be taken into consideration. In the best hands, it is probably justifiable to remove all nodules routinely. In any event, it is desirable to remove all nodular goiters with any substernal extension, all those which have recently increased in size, all those that are very large, those which produce pressure symptoms and those which are accompanied by enlargement of the lymph glands in the neck. Subtotal thyroidectomy should be done even though there appears to be only a single nodule, because there are commonly smaller nodules (often microscopic) throughout the gland. When the enlargement is slight, it is perhaps best to let the patient himself make the decision, after all the facts have been placed before him. If he is carefully followed, thyrotoxicosis can be detected as soon as it appears, further enlargement can usually be prevented by the administration of iodine, and he may wish to run the risk of carcinoma developing.

ANOMALIES OF DEVELOPMENT

Anomalies of development can readily be understood if the embryologic origin of the thyroid as an evagination of the primitive pharynx is borne in mind.[22] The thyroid tissue may fail to descend in whole or in part or may migrate to too low a level. Thus, it may be found in the nasopharyngeal, lingual, intralingual, sublingual, prelaryngeal, intratracheal, intraesophageal and mediastinal areas, and in very rare instances, as low as the diaphragm (goiter plongeant). The origins of lingual goiters, pyramidal lobes and substernal goiters are thus readily accounted for. Thyroglossal cyst is readily accounted for by the thyroid cells, in their descent, carrying down some pharyngeal cells, which give rise to a cyst. Such a cyst may communicate with the pharynx by way of the thyroglossal duct, which has failed to obliterate as it does during normal development, and with the skin through a permanent fistulous opening produced by spontaneous rupture or surgical incision. Such an opening is in the midline between the isthmus of the thyroid and the hyoid bone. There is some difference of opinion about the origin of lateral aberrant thyroid tissue. According to some observers, it arises from thyroid cells which come from the so-called fifth branchial pouch (ultimobranchial body).[23] According to hypothesis, these cells normally

21. Marine, David, and Kimball, O. P.: The Prevention of Simple Goiter in Man, J. Lab. & Clin. Med. **3**: 40 (Oct.) 1917.

22. Norris, E. H.: The Early Morphogenesis of the Human Thyroid Gland, Am. J. Anat. **24**: 443 (Nov.) 1918.

23. Leech, J. V.; Smith, L. W., and Clute, H. M.: Aberrant Thyroid Glands, Am. J. Path. **4**: 481 (Sept.) 1928.

descend and fuse with the anlage from the pharynx but take no part in the formation of the parenchyma of the thyroid. Failing to descend they may give rise to embryonic rests, which later develop into lateral aberrant thyroid tissue. This gives rise to tissue of a low grade of malignancy, which is usually of the nature of papillary cystadenoma. According to other observations, lateral aberrant thyroid tissue arises by separation from the main body of the thyroid. In rare instances thyroid tissue is found in teratoma, especially in the ovary. The thyroid tissue in teratoma may function. There is an instance on record in which it was responsible for the symptoms of exophthalmic goiter.

THYROIDITIS

Thyroiditis is a rare disease and may be acute, subacute or chronic and may be suppurative or nonsuppurative.[24] It may arise from a distant focus of infection or from a focus in neighboring structures of the neck. Infection may be introduced at the time of operation and give rise to postoperative thyroiditis. Any organism may infect the gland. The milder forms of infection may go unrecognized. Redness, swelling and tenderness of the skin over the thyroid, together with fever, suggest the presence of thyroiditis. Recurrent attacks of the noninflammatory variety may be noted, although one attack may completely destroy the gland and result in the development of myxedema. Tuberculosis of the gland is very rare and always secondary to tuberculosis elsewhere. Infection with pyogenic organisms may result in single or multiple abscesses or suppuration of the whole gland, usually associated with fever and often with a sudden onset. Abscesses should be drained because of the danger of spread of an infection into the mediastinum and along the fascial layers of the neck. Abscesses of the thyroid may compress the trachea, and relief may follow tracheotomy. The redness, swelling, tenderness and fever that sometimes accompany necrosis of thyroid tissue in patients with carcinoma may lead to a mistaken diagnosis of thyroiditis. The end result of thyroiditis is usually hypothyroidism, the extent of which is related to the amount of gland destroyed.

Struma lymphomatosa[25] and Riedel's struma are classified under the heading of chronic thyroiditis. Struma lymphomatosa occurs in older people and almost entirely in women. It is characterized by a rapid, firm swelling of the gland. It is usually bilateral, and the shape of the gland conforms more or less to the normal contour. The gland is hard and divided into lobules by dense bands of fibrous tissue. It shows numerous areas of lymphoid tissue with germinal centers and a few multinuclear giant cells. The gland may compress the trachea, although tracheotomy is rarely necessary. Subtotal thyroidectomy is indicated.

In Riedel's struma there is rapid, firm swelling of the gland, producing hard, woody thyroiditis. About half of the patients are men. In about half of the patients the process is unilateral. The gland is irregular and bound down to surrounding structures, giving rise, as a rule, to a preoperative diagnosis of carcinoma. However, there is no involvement of the skin or of the regional lymph nodes. As the disease progresses, there may develop compression of the trachea with asphyxia, hoarseness, dysphagia and involvement of the great vessels. Tracheotomy is necessary in about one fifth of the cases. Microscopically, the gland is largely replaced with dense fibrous tissue containing an occasional lymphoid follicle and some foreign body giant cells. As much of the mass should be removed surgically as possible.

Various types of involvement of the thyroid by Trypanosoma cruzi have been described in South America by Chagas.

NEW GROWTHS

The best review of the subject is given by Pemberton.[26] The ratio of malignant to benign tumors of the thyroid at the Mayo Clinic is about 4.9 per cent. Carcinoma of the thyroid may occur at any age but is most common between the ages of 40 and 70 years. The average age for men is about 53 years and for women about 48 years. The ratio of males to females in the experience of the Mayo Clinic is about 1 to 1.74.

Carcinoma of the thyroid almost always arises from a preexisting adenoma, although in rare instances it may develop in a gland involved in exophthalmic goiter. The diagnosis is not suspected before operation in about 60 per cent of the cases.

Papillary adenocarcinoma is of a low grade of malignancy and carcinoma in adenoma is of a slightly higher grade, while diffuse adenocarcinoma represents "the acute fulminating malignant growths of the thyroid gland."

Squamous epithelioma and sarcoma are very rare and very highly malignant. It is uncertain whether they arise from extensions from the esophagus, trachea or thyroglossal duct or directly from the thyroid by metaplasia of the epithelium.

Malignant change of the thyroid is most commonly confused with Riedel's struma, struma lymphomatosa and hemorrhagic adenoma. In the early stages it can be diagnosed only on histologic examination.[27] As the disease progresses, "the history of recent increase in the size of a pre-existing adenoma, the recent development of a tumor of the thyroid gland, a complaint of a sense of pressure in the neck, often out of proportion to the size of the tumor and the finding on palpation of a thyroid tumor that is firmer, more nodular and relatively more firmly fixed than that usually encountered in benign goiters, are all suggestive evidence. . . . Hoarseness and a fixed vocal cord in the absence of syphilis, aortic aneurysm or mitral stenosis are almost pathognomonic of malignancy." There is uncertainty about what constitutes microscopic evidence of malignancy. Invasion of blood vessels appears to be an absolute criterion but, according to Pemberton,[26] is not necessary for diagnosis, anaplasia and dedifferentiation being adequate evidence, as they are for carcinoma elsewhere in the body.

Whenever feasible, the tumor should be removed, and if complete removal is impossible, the operation should be followed by roentgen ray or radium treatment. If the growth is inoperable, radiation therapy is used alone. Complete fixation to surrounding structures of the neck and the presence of distant metastases are contraindications to operation. Enlargement of cervical lymph nodes also constitutes a contraindication except in the case of the slowly growing papillary adenocarcinoma.

24. Clute, H. M.: Thyroiditis—Simple, Suppurative and Chronic, Tr. Am. A. Study Goiter, 1931, p. 136.
25. Joll, C. A.: The Pathology, Diagnosis and Treatment of Hashimoto's Disease (Struma Lymphomatosa), Brit. J. Surg. **27**: 351 (Oct.) 1939.
26. Pemberton, J. deJ.: Malignant Lesions of the Thyroid Gland: A Review of Seven Hundred and Seventy-Four Cases, Tr. Third Internat. Goiter Conf. & Am. A. Study Goiter, 1938, p. 154.
27. Graham, Allen: Nodular Goiters: Their Relation to Neoplasia, Am. J. Surg. **7**: 163 (Aug.) 1929.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

HANOVIA AERO-KROMAYER LAMP MODELS S-2202, S-2203 ACCEPTABLE

Manufacturer: The Hanovia Chemical & Mfg. Company, Newark, N. J.

The Hanovia Aero-Kromayer Lamp is described by the firm as "A super high pressure quartz mercury vapor arc lamp of the activated electronic self-lighting type which is recommended for therapeutic use when local applications of ultraviolet radiation are required." Model S-2202 is for use with direct current, and model S-2203 operates on alternating current.

Fig. 1.—Hanovia Aero-Kromayer Lamp.

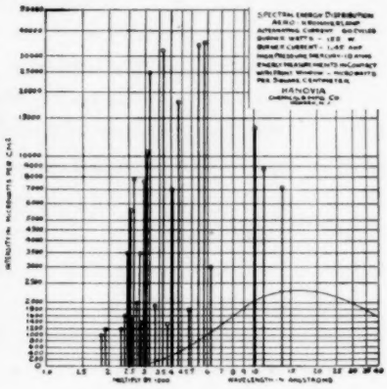

Fig. 2.—Spectral energy distribution curve.

A fused quartz, C-shaped burner containing mercury which vaporizes completely to a pressure of ten atmospheres during operation, a starting gas and activated electronic type electrodes comprise the lamp proper; the burner is completely enclosed within a metal housing provided with a fused quartz window. Another housing, which further encloses the burner unit, is said by the firm to provide forced draft cooling and partial removal of infra-red radiations and to be adapted for the handling and support of applicators for the conduction of the ultraviolet radiation into body cavities. Elimination of water for cooling, the decrease in the mercury content of the burner and complete vaporization of the mercury reduce weight and facilitate handling.

The lamp is used manually. An automatically controlled red warning light mounted on the control cabinet indicates when the mercury is completely evaporated and the lamp is ready for application.

The data in table 1 as to the electrical characteristics of the lamp were submitted by the firm.

TABLE 1.—*Electrical Characteristics of the Lamp*

Supply	Alternating Current Model S-2203	Direct Current Model S-2202
Supply voltage	115 (105-125)	115 (105-130)
Fuse size	20 amperes	10 amperes
Starting current	12 amperes	4 amperes
Operating current	5 amperes	2.5 amperes
Wattage	230 watts	340 watts
Burner		
Burner voltage	135 volts	65 volts
Starting current	4.2 amperes	4 amperes
Operating current	1.6 amperes	2.5 amperes
Wattage	160 watts	160 watts
Motor		
Wattage	25 watts	25 watts

The lamp produces the familiar mercury arc in quartz spectrum, but the spectral energy distribution differs from that of the usual air cooled or water cooled lamps because of the higher pressure of the mercury vapor in the Aero-Kromayer.

In the Council's investigation of the physical characteristics of the lamp it was found that the relative spectral intensities were similar to those of any hot quartz lamp, differing mainly in having a brighter continuous background. The integrated ultraviolet total intensity of wavelengths 3,132 angstroms and shorter was measured with a balanced thermopile and filter.

Table 2 gives the total radiant power of wavelengths 3,132 angstroms and shorter in microwatts per square centimeter in the center of the light beam at various distances measured from the front window of the lamp when operated on 115 volts alternating current.

Presumably owing to internal reflection from the aluminum metal support, with the compression window in place the intensity was found to be practically unchanged in the center of the beam. With the compression window in place (at a distance of 1.5 cm. in front of the outer lamp window) the intensity was about 150,000 microwatts per square centimeter, requiring about one-third second to produce a minimum perceptible erythema. However, since the irradiated field is spotted, this is only an average value.

Two series of erythema tests were made on the forearm at the compression window (but not under compression) with exposures of one, two and three seconds. In one series of trials the erythema resulting from the one second exposure disappeared in less than twenty-four hours. In another series, part of the irradiated field for one second's exposure continued red for two days, apparently from unequal irradiation. The longer exposures produced a second degree erythema with perceptible pigmentation. The erythema tests therefore confirm the radiometric measurements and calculations, showing that, at the compression window, the ultraviolet radiation intensity of wavelengths 3,132 angstroms and shorter is very high.

Clinical investigation of the lamp showed that the rim of the outer window became quite hot after the lamp had been in use a few seconds. When treating lesions requiring compression it is necessary to use some material which does not conduct heat at the periphery of the compression window. Some diseases which ordinarily respond to ultraviolet rays were treated with the Hanovia Aero-Kromayer Lamp. The results were the same as those obtained with other sources of ultraviolet generators in which the physical characteristics correspond to those of the lamp under investigation.

TABLE 2.—*Total Radiant Power*

Distance from front window	40 cm.	30 cm.	15 cm.	4 cm.	1.5 cm.
Intensity, microwatts per square centimeter	790	1,440	4,800	46,000	155,000

The Council on Physical Therapy voted to accept the Hanovia Aero-Kromayer Lamp, Models S-2202 and S-2203, for inclusion on its list of accepted devices.

Early Reference to Insanity in the Bible.—The earliest reference to insanity in the old Bible (1451 B. C.) is probably that in Deuteronomy 28:28, where it says, "The Lord shall smite thee with madness, and blindness, and astonishment of heart," a threatened punishment for those who disobey the commands of God. Among the early Hebrew accounts are the recurrent attacks of melancholia and mania terminating in the suicide of Saul (1097-1058 B. C.), King of Israel, the simulated insanity of David, and the lycanthropic mental illness of Nebuchadnezzar of Babylonia.—Lewis, Nolan D. C.: A Short History of Psychiatric Achievement, New York, W. W. Norton & Co., Inc., 1941.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, AUGUST 9, 1941

THE NEW PHYSIOLOGIC SURGERY ON THE HEART

Until its modern period surgery was largely concerned with the removal of diseased parts of the human body. This type of surgery, while beneficial, is essentially the surgery of mutilation. No doubt legs will continue to be amputated, appendixes will be removed, parts of the brain will be ablated. Nevertheless the present trend of surgery is reconstructive, plastic, physiologic. The interesting surgery on the heart now under investigation in several institutions illustrates this exploration toward future progress.

The heart is anchored in the body by the great vessels at its base. This anatomic arrangement deprives the organ of continuity with adjacent tissues; physiology teaches that continuity is essential for the development of blood vessels from one structure to another. If continuity is given between myocardium and the parietal pericardium, mediastinal or omental fat or skeletal muscle, anastomoses will develop between the coronary arteries and the arteries of the grafted tissues. Beck and his associates [1] in Cleveland have demonstrated such anastomoses. These anastomotic channels are readily seen in specimens that were injected and cleared. The largest anastomoses measure about 1 mm. in diameter. The vessels of the grafted tissues can be injected from the coronary arteries, and the coronary arteries can be injected from the grafts, thus establishing the existence of continuity. The grafts, it is reported, do not in any way interfere with the beating of the heart.

As pointed out by Beck, a second anatomic arrangement that adds to the ravages of coronary artery disease can be found in the capillary bed of each coronary artery. The right coronary artery, the descending ramus of the left coronary artery and the circumflex ramus of the left coronary artery possess capillary beds that practically do not anastomose one with another. If the beds were freely united, occlusive disease of any one artery could be better tolerated.

The Cleveland investigators have shown that intercoronary communications can be produced in two ways. One method, and this is not a surgical method, is by occlusion of a coronary artery. They have shown experimentally that, if a normal heart tolerates occlusion of a major coronary artery, intercoronary communications always develop and a common coronary bed is produced. While the stimulus of arterial occlusion cannot be used as a surgical method to produce intercoronary communications, it can be used effectively in an indirect manner. Consideration must be given to the two destructive factors that accompany coronary artery occlusion. One of these is death of myocardium or the formation of an infarct. The other is ventricular fibrillation, which produces heart failure and total death of the body. These destructive factors are both due to lack of oxygen. They can be prevented by a relatively small amount of oxygenated blood delivered through the occluded artery. This relatively small amount of blood need not be enough to make possible active contraction of the myocardium but just enough to preserve the viability of the heart muscle and to prevent it from changing to scar tissue. The Western Reserve investigators have shown that a sufficient quantity of blood can be delivered to the occluded artery by surgical methods to prevent death of myocardium and to prevent ventricular fibrillation. If the heart can be made to survive the critical period following occlusion, the stimulus of occlusion becomes effective. Ultimately these two destructive factors disappear as a common coronary bed comes into existence.

The second method by which a common coronary bed can be produced is by inflammation. The inflammatory agent may be mechanical or chemical. Beck used abrasion of the surface of the heart and powdered beef bone as a foreign body to produce inflammation. Recently Stanton, Schildt and Beck [2] made measurements of the effect of epicardial abrasion and also the effect of various chemical agents in reference to the development of intercoronary communications. They found that abrasion of the heart alone gave a definite protection to the heart. It reduced the mortality from 70 per cent in 50 normal hearts in which the descending ramus of the left coronary artery was ligated at its origin to 38 per cent in 50 hearts in which the same artery was ligated but in which the surface of the heart had been abraded at a previous operation. Abrasion opened up intercoronary communications and reduced the size of the infarct. Indeed, in some of the specimens an infarct did not develop after ligation of the descending artery.

1. Beck, C. S.: Development of a New Blood Supply to the Heart by Operation, Ann. Surg. **102**: 801 (Nov.) 1935. Beck, C. S., and Tichy, V. L.: The Production of a Collateral Circulation to the Heart, Am. Heart J. **10**: 849 (Oct.) 1935. Mautz, F. R., and Beck, C. S.: The Augmentation of Collateral Coronary Circulation by Operation, J. Thoracic Surg. **7**: 113 (Dec.) 1937. Beck, C. S.: Further Data on the Establishment of a New Blood Supply to the Heart by Operation, ibid. **5**: 604 (Aug.) 1936.

2. Stanton, E. J.; Schildt, P. J., and Beck, C. S.: Abrasion of Surface of Heart and Effect on Intercoronary Communications, Am. Heart J., to be published.

An infarct always develops in a normal heart after this artery is ligated. It was shown that intercoronary communications developed as early as five to seven days after the surface of the heart was abraded. Certain chemical agents produce a profound reaction on the surface of the heart, and their use is not without danger. Calcium and magnesium silicate in fibrous form in small quantities was found to produce the most desirable reaction. A small amount of this substance placed on the surface of the heart produces a reaction which seems to aid the development of intercoronary channels. The mortality in such experiments following ligation of the descending ramus is about 20 to 30 per cent. In some of these specimens there is no infarct.

Application of some of these new physiologic facts to the surgery of coronary disease was first made by Beck, it is reported, on Feb. 13, 1935. The patient was a farmer. He became totally crippled by coronary artery disease. The patient, who considered his life intolerable, tolerated the operation, recovered and is now employed as a farm hand. This patient believes that he is cured. Thirty such patients were operated on. All were considered bad risks for any operation, and 10 were lost in the postoperative period. Of the 20 who survived, 17 continue to live and almost all consider themselves improved. The beneficial result in some of these cases has been almost incredible. The data obtained from this study group have been encouraging. Many of the patients stated that they felt better as early as one week after operation. The earliest that Beck and Tichy could demonstrate a watery dye passing from grafts to heart was two or three weeks after operation. This early improvement as stated by the patients was discounted at that time because there was no experimental evidence to support it. Now, however, this early clinical improvement can be accepted because intercoronary communications can be demonstrated within a few days after operation and these intercoronary channels can account for the early clinical improvement. Indeed, early clinical improvement is now to be expected after operation.

The results of these pioneer operations have just been published in the *Journal of Thoracic Surgery*.[3] It has also been shown by the Western Reserve investigators that the heart maintains its protection over a period of months after it has been prepared by operative methods, even though arterial occlusion has not been added to the experiment. From these experiments it would appear that the operation has prophylactic value.

Coronary artery disease cannot be eradicated by operation. Every procedure must therefore be considered in terms of improvement following operation rather than cure of the disease. After muscle degenerates into scar tissue, the infarct cannot be changed back to muscle. Some patients may not appear to be helped by the operation because the destructive process of the disease in the coronary arteries may be more rapid than the reconstructive process following the operation. These limitations must be considered but apparently should not necessarily preclude application of the operation in the treatment of coronary artery disease and angina pectoris.

Experimentally in animals it has been shown that the normal heart can tolerate the operation almost without any risk. If the disease itself is not totally incapacitating, the risk should not be much greater than that of many other operations. Even if the disease is totally incapacitating, the Cleveland surgeons say the operation can be done. The patients selected by Feil were totally incapacitated, and even in this group the mortality was not forbidding. Possibly a more limited procedure could be applied to patients who have advanced disease.

3. Feil, Harold, and Beck, C. S.: Coronary Sclerosis and Angina Pectoris, J. Thoracic Surg. **10**: 529 (June) 1941.

RELATION OF CHEMICAL STRUCTURE OF MORPHINE DERIVATIVES TO ADDICTION LIABILITY

Many agencies have been interested in the solution of the problem of drug addiction. The Division of Mental Hygiene of the United States Public Health Service includes among its functions (1) the administration of two federal institutions for the confinement and treatment of persons addicted to the use of habit forming drugs, (2) the conduct of studies dealing with the nature of drug addiction and (3) possible methods of treatment and rehabilitation of persons addicted to the use of habit forming drugs, and (4) the supervision and furnishing of the medical and psychiatric services in the federal prison system. The National Research Council, the Rockefeller Foundation, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia and the University of Michigan are some of the other institutions which participate in the prosecution of the studies.

The purpose of these combined studies has been to find some means of reducing or correcting the evils of drug addiction. The assumption has been made that some persons possess receptors which, when combined with a chemical unit of an addictive drug, give rise to a sense of euphoria. Desirable therefore was separation chemically, if possible, of the addiction property of morphine from its analgetic attributes. A systematic study was made of a series of modifications of the morphine molecule, followed by a careful physiologic study and application to man of those substances which give definite indications of value.

A series of sixteen drugs, all modifications of the morphine molecule and of known chemical composition,

have been studied in man. One of the chemical difficulties in this research has been to provide drugs which would prolong the pain control factor so as to reduce the need for repeated dosage and at the same time to eliminate the fraction responsible for euphoria.

Much of the clinical work in this connection is being conducted at the U. S. Public Health Service Hospital, Lexington, Ky., an institution suited for the prosecution of this type of investigation because of the complete control of its patients. The approach to the problem, according to Himmelsbach,[1] was based on the hypothesis that variations in chemical structure often cause variations in physiologic effects, and that if the latter can be identified with certain portions of the morphine molecule it might be possible to suppress or eliminate undesirable actions and at the same time retain or improve the desirable effects. The method employed consisted of selection of addicts with active physical dependence,, preliminary stabilization of patients on morphine, replacement of morphine by another substance for a period of at least one week, and withdrawal of the substituted drug. In this way, according to Himmelsbach, one may learn whether or not a chemical substance will satisfy preestablished physical dependence. The maintenance of physical dependence by a substituted drug is considered to indicate that it is capable of producing addiction. No nonaddictive drug has been found to support physical dependence. The physical dependence already established to morphine apparently becomes adapted to the substitute, for, on withdrawal, detectable and self-consistent dissimilarities have been found in the abstinence syndromes of drugs studied. These dissimilarities are based on alterations in chemical structure. The abstinence syndrome which appears after withdrawal of the substituted drug is thought to be the equivalent of that which would occur were addiction to the substituted drug primary instead of secondary.

The phenanthrene derivatives of opium experimented with were dihydromorphine, alpha-isomorphine, dihydro-alpha-isomorphine, dihydromorphinone, dihydrodesoxy-morphine-D, codeine, dihydrocodeine, isocodeine, dihydroisocodeine and dihydrodesoxycodeine-D.

The results obtained by Himmelsbach are qualitatively similar to those of Small and Eddy.[2] By means of substitution technic, data were obtained on the potency and duration of the physical dependence action of each of ten related drugs of the morphine, codeine series. From comparisons of pairs of drugs differing from each other in only one structural respect it would appear that, as far as physical dependence action is concerned, (*a*) methylation of the phenolic OH reduces potency and prolongs action, (*b*) replacement of the alcoholic OH by H or O increases potency and shortens the action, (*c*) spatial shift of the alcoholic OH results in irregular effects and (*d*) saturation of the C-7, 8 double bond tends to increase both the potency and the duration of action. None of the types of chemical modifications mentioned in this report caused reductions in both duration and intensity of physical dependence action. It is nonetheless reasonable to expect that this research will eventually lead to the discovery of a substitute which, while retaining the analgetic attributes of morphine, would possess the minimum of its addiction property.

1. Himmelsbach, C. K.: Studies of Certain Addiction Characteristics of (*a*) Dihydromorphine ("Paramorphan"), (*b*) Dihydrodesoxymorphine-D ("Desomorphine"), (*c*) Dihydrodesoxycodeine-D ("Desocodeine") and (*d*) Methyldihydromorphinone ("Metopon"), J. Pharmacol. & Exper. Therap. **67**: 239 (Oct.) 1939; The Effects of Certain Chemical Changes on the Addiction Characteristics of Drugs of the Morphine, Codeine Series, ibid. **71**: 42 (Jan.) 1941.

2. Small, L. F., and Eddy, N. B.: Some Relationships Between Chemical Constitution and Pharmacological Action in the Morphine Series, in Small, L. F.; Eddy, N. B.; Mosettig, E., and Himmelsbach, C. K.: Studies on Drug Addiction with Special Reference to Chemical Structure of Opium Derivatives and Allied Synthetic Substances and Their Physiological Action, Pub. Health Rep., 1938, supp. 138.

Current Comment

SCIENCE IN A TROUBLED WORLD

Amidst the rubble of bombings, the distinguished physiologist and member of Parliament Dr. A. V. Hill[1] addressed the House of Commons. Dr. Hill is uneasy about certain tendencies that have developed in science in his country as they have in ours. A growing tendency for political considerations to exercise an influence on science is viewed with alarm by every scientist. "In order to preserve the integrity of science in our own country," Dr. Hill states, "it is very important that those strong independent scientific bodies should be maintained: and for the sake of international scientific relations it is desirable that in other countries also, so far as we can influence them, the domination of the state over science should be tempered by public appreciation of the part played by independent scientific agencies and institutions." The British spokesman recognizes the importance, indeed the necessity, of scientific organizations within the framework of government. Anent the hazard of government subsidized research he mentioned "the danger that he who pays the piper may call the tune, and that research may be required to be devoted primarily to objects which the politician, or the civil servant, regard for the moment as of national importance." To avoid the evils of this he calls for a powerful buffer to prevent the state from interfering with the integrity and independence of research. Dr. Hill said, in conclusion, "Blessed are they who remain innocently in their laboratories and grumble: for it is a thankless task to get things right. . . . All we ask is that we should be considered as equals in a common task—not merely as superior technicians paid to dish up the magic which you order."

1. Hill, A. V.: Science, National and International, and the Basis of Cooperation, Science **93**: 579 (June 20) 1941.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

ARMY RESERVE OFFICERS ORDERED TO ACTIVE DUTY

WAR DEPARTMENT

The following additional medical reserve corps officers have been ordered to extended active duty by the War Department, Washington, D. C.:

ADAMS, John E., 1st Lieut., Los Angeles.
ALDES, John H., 1st Lieut., Cincinnati.
ANDERSON, Andrew Russell, 1st Lieut., Baltimore.
APRILE, Ignatius Joseph, 1st Lieut., Jackson Heights, L. I., N. Y.
BAKER, William Nowers, 1st Lieut., Pueblo, Colo.
BERK, Jack Edward, 1st Lieut., Philadelphia.
BERK, Morris David, Captain, Pompton Lakes, N. J.
BERMAN, Reuben, Captain, Minneapolis.
BETHEA, John Hardee, Captain, New Orleans.
BOEDEKER, Roy Vincent, Captain, Russellville, Ky.
BURNS, Harry, Captain, Fort Des Moines, Iowa.
BYRNE, Walter Robbins, 1st Lieut., Russellville, Ky.
CARBONEL, Arthur Joseph, 1st Lieut., Washington, D. C.
CICCONE, Roy, Captain, Boston.
CRUTCHER, John Sims, Jr., Major, Athens, Ala.
DEEMS, Myers Bowman, 1st Lieut., St. Louis.
DESSEN, Edgar Lee, 1st Lieut., Philadelphia.
EAGLES, Archie Y., 1st Lieut., Baltimore.
EVANS, William Dustin, 1st Lieut., Los Angeles.
FARRIOR, James Harvey, 1st Lieut., Montgomery, Ala.
FRENCH, Lyle Albert, 1st Lieut., Minneapolis.
FISHER, Rowan Elliott, 1st Lieut., Dallas, Texas.
FOSTER, Rae N., 1st Lieut., John Day, Ore.
GAMBLE, Jess Franklin, 1st Lieut., Alexandria, Va.
GODARD, Clarence Harley, 1st Lieut., Los Angeles.
GRAHAM, John Glenwood, Jr., 1st Lieut., University City, Mo.
HAINESWORTH, Winston Clarkson, 1st Lieut., Washington, D. C.
HARRIS, Major Haymond, 1st Lieut., Decatur, Ga.
HOFFMAN, I. Louis, Captain, Brooklyn.
HOURICAN, Donald Joseph, 1st Lieut., Pittsburgh.
HUGHES, Jack Robert, 1st Lieut., San Francisco.
JESSER, Joseph Herman, 1st Lieut., Chicago.
JESURUN, Harold Mendez, 1st Lieut., Brooklyn.
JOHNSON, Elgie Karl, 1st Lieut., Columbus, Ohio.
JONES, Harry Douglas, 1st Lieut., Nashville, Tenn.
KAMINSKI, Paul Joseph, 1st Lieut., Baltimore.
KANTOR, George J., Captain, Brooklyn.
KENNEDY, Paul Andrew, 1st Lieut., Scranton, Pa.
KERRON, Seth Metcalfe, Major, Vancouver, Wash.
LATIMER, John Wilmer, Jr., 1st Lieut., Washington, D. C.
LEONARD, William Parker, Jr., 1st Lieut., Talbotton, Ga.
LIHN, Barney, 1st Lieut., Vineland, N. J.
MALONEY, John Joseph, 1st Lieut., Washington, D. C.
MARKLE, Philip Metric, Captain, Memphis, Tenn.
NASH, Joseph, 1st Lieut., New York.
NEWMAN, Robert Lewis, 1st Lieut., Kansas City, Kan.
NOLAN, Oscar Frederick, Captain, San Francisco.
O'CONNELL, John Richards, 1st Lieut., Fort Dodge, Iowa.
PRATT, Thomas Dennie, 1st Lieut., Brookline, Mass.
RAPEE, Lawrence Albert, 1st Lieut., Washington, D. C.
RIESENMAN, Francis Regis, 1st Lieut., Franklin, Pa.
ROBERTS, Harold Kersey, 1st Lieut., St. Louis.
RODDA, John S., 1st Lieut., Oakland, Calif.
ROSENFIELD, Richard E., 1st Lieut., Pittsburgh.
ROSS, Donald, 1st Lieut., Chicago.
ROULHAC, George Erwin, 1st Lieut., St. Louis.
RUDI, Herbert John, Captain, St. Louis.
SACK, Samuel Senior, Captain, Brooklyn.
SAWYER, Logan Everett, 1st Lieut., Baltimore.
SHIFFLER, Harry Kirby, 1st Lieut., Des Moines, Iowa.
SILVERSTONE, Eugene Henry, 1st Lieut., Iowa City.
SIMMONS, Melvin Morris, 1st Lieut., Nashville, Tenn.
SMITH, Robert Cathcart, 1st Lieut., Baltimore.
STEVENS, Lawrence Hefron, Captain, St. Louis.
THORNE, Lewis, 1st Lieut., New Haven, Conn.
TILLMAN, Paul Frederick, Captain, Northport, L. I., N. Y.
WILKINSON, Thomas Charles, Captain, Pittsburgh.
WOLPAW, Ralph, 1st Lieut., Cleveland.
YURICK, Edward Andrew, Captain, Cleveland.

Orders Revoked

EVANS, William Dustin, 1st Lieut., Los Angeles.
JACOBSON, Alan, 1st Lieut., Baltimore.

SECOND CORPS AREA

The following additional medical reserve corps officers have been ordered to active duty by the Commanding General, Second Corps Area, which comprises the states of New York, New Jersey and Delaware:

ABERS, Bernard D., 1st Lieut., Jersey City, N. J., Advanced Flying School, Selma, Ala.
ABRAHAM, Albert E., 1st Lieut., Arlington, N. J., Air Base, Tallahassee, Fla.
ABRAHAMS, Joseph, 1st Lieut., Brooklyn, Fort Jackson, S. C.
ALVAREZ, Lawrence J., 1st Lieut., Brooklyn, Camp Upton, N. Y.
AMAR, Vincent F., 1st Lieut., Yonkers, N. Y., Advanced Flying School, Albany, Ga.
AMATO, Romelo J., 1st Lieut., Newark, N. J., Air Base, Jackson, Miss.
BAKER, Augustus L., Jr., 1st Lieut., Montclair, N. J., Camp Shelby, Miss.
BALDWIN, John F., 1st Lieut., West Englewood, N. J., Fort Dix, N. J.
BANTA, Raymond E., 1st Lieut., Tenafly, N. J., Fort Jay, N. Y.
BARMEYER, George H., Jr., 1st Lieut., Bayside, N. Y., Air Base, Savannah, Ga.
BARRETT, George S., 1st Lieut., Scotia, N. Y., Carlisle Barracks, Pa.
BASHEIN, Hyman, Captain, Brooklyn, Advanced Flying School, Selma, Ala.
BEACHER, Milton D., 1st Lieut., Brooklyn, Air Base, Augusta, Ga.
BEAVERS, Alonzo J., Jr., 1st Lieut., Valhalla, N. Y., Air Base, Savannah, Ga.
BENNY, John M., 1st Lieut., Buffalo, Fort Niagara, N. Y.
BERLIN, Walter, 1st Lieut., Jersey City, N. J., Camp Shelby, Miss.
BLACK, Asher, 1st Lieut., Solvay, N. Y., Fort Ontario, N. Y.
BOBBETT, Gordon H., 1st Lieut., Auburn, N. Y., Fort Ontario, N. Y.
BOORSTEIN, Maccabae, 1st Lieut., New York, Fort Jackson, S. C.
BOYD, Hamilton, Jr., 1st Lieut., Kingston, N. Y., Elgin Field, Valparaiso, Fla.
BRANDES, Peter, 1st Lieut., Malone, N. Y., Plattsburg Barracks, N. Y.
BREEN, Victor M., 1st Lieut., Buffalo, Fort Niagara, N. Y.
BROADMAN, Sylvan A., 1st Lieut., New York, Fort Hancock, N. J.
BROWN, Kenneth L., 1st Lieut., Buffalo, Fort Niagara, N. Y.
BURSON, Leonard C., 1st Lieut., Rockaway Park, N. Y., Fort Jackson, N. Y.
CALABRESE, Dino D., 1st Lieut., Ridgefield, N. J., Camp Shelby, Miss.
CAMPBELL, Donald, 1st Lieut., New York, Fort Jackson, S. C.
CARLOZZI, Michael, 1st Lieut., Brooklyn, Camp Shelby, Miss.
CAYAVES, Paul G., 1st Lieut., New York, Camp Shelby, Miss.
CEBULA, Jerome M., 1st Lieut., Brooklyn, Advanced Flying School, Selma, Ala.
CHILDS, Milford N., 1st Lieut., Buffalo, Fort Niagara, N. Y.
CLEMENTS, James J., 1st Lieut., Syracuse, N. Y., Fort Ontario, N. Y.
COLE, Charles H., 1st Lieut., Ossining, N. Y., Camp Shelby, Miss.
COOPER, George M., 1st Lieut., Buffalo, Fort Niagara, N. Y.
CORLESS, Joseph F., 1st Lieut., West New York, N. J., Air Base, Orlando, Fla.
COSGROVE, Robert A., Captain, Jersey City, N. J., Fort Du Pont, Del.
CROZIER, Dan, 1st Lieut., Brooklyn, Fort Hancock, N. J.
CUTLER, Martin, 1st Lieut., Brooklyn, Air Base, Baton Rouge, La.
DANIEL, Walter A., 1st Lieut., Brooklyn Headquarters 2d Military Area, New York.
DANZIS, Louis, 1st Lieut., Irvington, N. J., Camp Shelby, Miss.
DAVIS, Isidore, 1st Lieut., Brooklyn, Advanced Flying School, Albany, Ga.
DeHOFF, John B., 1st Lieut., New York, N. Y., Air Base, West Palm Beach, Fla.
DELAGI, Edward F., 1st Lieut., New York, Fort Jackson, S. C.
DeMARCO, Luciano E., 1st Lieut., Newark, N. J., Camp Shelby, Miss.
DENGROVE, Edward, 1st Lieut., Jersey City, N. J., Air Base, West Palm Beach, Fla.
DOLGOW, Joseph, 1st Lieut., Brooklyn, Air Base, Augusta, Ga.
DORF, Victor, 1st Lieut., Brooklyn, Camp Shelby, Miss.
DREXLER, Milton, 1st Lieut., New York, Camp Shelby, Miss.
EDELMAN, Robert M., 1st Lieut., Richmond Hill, L. I., 38th Division, Camp Shelby, Miss.
ENGELHARD, George E., 1st Lieut., Arlington, N. J., Pine Camp, N. Y.
ERBER, Leonard B., 1st Lieut., Atlantic City, N. J., Camp Shelby, Miss.
FABIAN, Norman, 1st Lieut., Poughkeepsie, N. Y., Air Base, Savannah, Ga.

FINKLESTEIN, Howard E., 1st Lieut., Woodhaven, N. Y., Camp Claiborne, La.
FISHBERG, Archibald, 1st Lieut., New York, Camp Shelby, Miss.
FORD, John H., Jr., 1st Lieut., Syracuse, N. Y., Carlisle Barracks, Pa.
FORST, Arthur, 1st Lieut., New York, Camp Shelby, Miss.
FOX, Lester, 1st Lieut., Brooklyn, Fort Bragg, N. C.
FUCHS, Isidor Irving, 1st Lieut., Brooklyn, Fort Hancock, N. J.
FULLER, Robert M., 1st Lieut., New York, Pine Camp, N. Y.
GERBER, Howard R., 1st Lieut., Brooklyn, Advanced Flying School, Albany, Ga.
GERHARDT, Paul E., 1st Lieut., Irvington, N. J., Fort Jackson, S. C.
GOLBY, Saul, 1st Lieut., Brooklyn, Air Base, Augusta, Ga.
GORDON, Irving Jacob, 1st Lieut., Flushing, N. Y., Camp Stewart, Ga.
GOTTLIEB, Morris, 1st Lieut., Ventnor City, N. J., Air Base, Orlando, Fla.
GRABER, Irving, 1st Lieut., Brooklyn, Air Base, West Palm Beach, Fla.
GREASER, George L., 1st Lieut., Johnson City, N. Y., Fort Niagara, N. Y.
GREIFINGER, William, 1st Lieut., Newark, N. J., Fort Hamilton, N. Y.
GRUBIN, Charles J., 1st Lieut., Brooklyn, Camp Blanding, Fla.
HEAD, Joseph A., 1st Lieut., Syracuse, N. Y., Pine Camp, N. Y.
HERMAN, Seymour J., 1st Lieut., Brooklyn, Camp Stewart, Ga.
HICKS, Andrew R., 1st Lieut., Mount Vernon, N. Y., Advanced Flying School, Albany, Ga.
HOCHMAN, David, 1st Lieut., Brooklyn, Air Base, Savannah, Ga.
HOFFMAN, Benjamin, 1st Lieut., Brooklyn, Camp Stewart, Ga.
HOROWITZ, Leo, 1st Lieut., Jersey City, N. J., Camp Shelby, Miss.
HUBBARD, Robert D., 1st Lieut., Camden, N. Y., Madison Barracks, N. Y.
HUMMEL, Frederick W., 1st Lieut., West Belmar, N. J., Camp Shelby, Miss.
INGRISANO, Louis A., 1st Lieut., Brooklyn, 114th Infantry, Fort Dix, N. J.
JAFFE, Bernard, 1st Lieut., New York, Advanced Flying School, Selma, Ala.
JANNARONE, Lewis H., 1st Lieut., Belleville, N. J., Fort Jackson, S. C.
JESURUN, Harold M., 1st Lieut., Brooklyn, Fort Bragg, N. C.
JONES, Courtland S., 1st Lieut., Buffalo, Fort Niagara, N. Y.
JONES, William F., 1st Lieut., Somerville, N. J., Air Base, Orlando, Fla.
JUVELIER, Bernard W., 1st Lieut., Buffalo, Fort Niagara, N. Y.
KAINE, Henry, 1st Lieut., New York, Fort Jackson, S. C.
KARP, Frank L., 1st Lieut., Long Beach, L. I., Fort Bragg, N. C.
KAYCOFF, Aaron J., 1st Lieut., Elizabeth, N. J., Air Base, Meridian, Miss.
KELLER, Paul D., 1st Lieut., Brooklyn, Camp Shelby, Miss.
KENT, Louis R., 1st Lieut., Port Washington, N. Y., Camp Shelby, Miss.
KLEMANN, Gilbert L., 1st Lieut., New Rochelle, N. Y., Air Base, Augusta, Ga.
KLIMASZEWSKI, Lucyan F., 1st Lieut., Syracuse, N. Y., Fort Dix, N. J.
KOCH, William J., 1st Lieut., Interlaken, N. J., Carlisle Barracks, Pa.
KRISCHER, Meyer I., 1st Lieut., Brooklyn, Fort Jackson, S. C.
KURLAND, Harry A., 1st Lieut., New York, Fort Jackson, S. C.
LAMBERTI, John J., 1st Lieut., Yonkers, N. Y., Air Base, Augusta, Ga.
LARKEY, Irving G., 1st Lieut., Newark, N. J., Fort Benning, Ga.
LAVIN, Paul R., 1st Lieut., Whitney Point, N. Y., Fort Niagara, N. Y.
LEAK, Glenn H., 1st Lieut., Buffalo, Fort Niagara, N. Y.
LENOBEL, Milton I., 1st Lieut., Brooklyn, Air Base, Augusta, Ga.
LETTERESE, Thomas G., 1st Lieut., New York, Fort Jackson, S. C.
LEIBENHAUT, Milton, 1st Lieut., Brooklyn, 38th Division, Camp Shelby, Miss.
LEVINE, Sanford, 1st Lieut., Brooklyn, Advanced Flying School, Selma, Ala.
LICKERMAN, Nathan, 1st Lieut., New York, Air Base, Jackson, Miss.
LIPARI, Michael, 1st Lieut., Hicksville, N. Y., Advanced Flying School, Albany, Ga.
LONDON, Ephraim J., 1st Lieut., Brooklyn, Fort Benning, Ga.
LOVELOCK, Francis J., 1st Lieut., New York, Fort Wadsworth, N. Y.
LYNCH, Thomas F., 1st Lieut., New York, Camp Upton, N. Y.
McDERMOTT, Kenneth J., 1st Lieut., Syracuse, N. Y., Fort Ontario, N. Y.
McVAUGH, Charles C., 1st Lieut., New York, Air Base, Tallahassee, Miss.
MARKS, Jerome L., 1st Lieut., New York, Fort Wadsworth, N. Y.
MAYBARDUK, Alexander P., 1st Lieut., New York, Camp Shelby, Miss.
MAYER, Victor, 1st Lieut., Brooklyn, Camp Blanding, Fla.
MELAVILLE, Eugene F., 1st Lieut., Rochester, N. Y., Fort Niagara, N. Y.
MEYER, Albert H., 1st Lieut., Brooklyn, Flying Cadet Examining Board, New York.
MERMELL, Lester, 1st Lieut., Middletown, N. Y., Induction Station, Fort Jay, N. Y.
MONACO, Saverio A., 1st Lieut., Newark, N. J., Fort Dix, N. J.
MORTON, Edward A., 1st Lieut., New York, Fort Jackson, S. C.
MUNRO, Howard F., Captain, Freeport, N. Y., Fort Jackson, S. C.
MURPHY, Arthur G., 1st Lieut., Montclair, N. J., Fort Monmouth, N. J.
MURPHY, George E., 1st Lieut., Paterson, N. J., Carlisle Barracks, Pa.
NEWELL, Robert B., 1st Lieut., Kenmore, N. Y., Fort Niagara, N. Y.
NEWMAN, Ernest B., 1st Lieut., Brooklyn, Camp Blanding, Fla.
NEIER, Charles R., 1st Lieut., Jamaica, N. Y., Camp Lee, Va.
NONAS, Gerson, 1st Lieut., Brooklyn, 8th Division, Fort Jackson, S. C.
NUSSBAUM, Herman, 1st Lieut., Welfare Island, N. Y., Elgin Field, Valparaiso, Fla.
OAKES, Alden B., 1st Lieut., Brooklyn, Air Base, Augusta, Ga.
O'CONNOR, Daniel J., 1st Lieut., Brooklyn, Air Base, Orlando, Fla.
PEIMER, Ralph, 1st Lieut., Paterson, N. J., Fort Dix, N. J.
PENNINGTON, Glenn W., 1st Lieut., New York, Camp Blanding, Fla.
PERSICO, Anthony J., 1st Lieut., New York, Advanced Flying School, Albany, Ga.
PETINGA, Thomas J., 1st Lieut., Atlantic City, N. J., Fort Du Pont, Del.
PLATT, Edward V., 1st Lieut., Haddon Heights, N. J., Camp Shelby, Miss.
RAUH, Albert E., 1st Lieut., New York, Induction Station, Fort Jay, N. Y.
REINUS, Francis Z., 1st Lieut., New York, Air Base, Augusta, Ga.
RITOTA, Michael C., 1st Lieut., Orange, N. J., Camp Shelby, Miss.
ROBBINS, Howard C., 1st Lieut., Bridgeton, N. J., Air Base, Savannah, Ga.
ROBERTS, Montague A., 1st Lieut., Englewood, N. J., Fort Hancock, N. J.
ROEMMELT, John C., Jr., 1st Lieut., Horseheads, N. Y., Carlisle Barracks, Pa.
ROGERS, Samuel L., 1st Lieut., Brooklyn, Air Base, Tallahassee, Fla.
ROOT, Nathan N., 1st Lieut., Kew Gardens, N. Y., Induction Station, Fort Jay, N. Y.
ROSEN, Bernard A., 1st Lieut., New York, Air Base, Meridian, Miss.
ROTHSTEIN, Daniel, 1st Lieut., Welfare Island, N. Y., Elgin Field, Valparaiso, Fla.
RUBENSTEIN, George, 1st Lieut., Dunkirk, N. Y., Fort Niagara, N. Y.
RUDOY, Martin, 1st Lieut., Brooklyn, 38th Division, Camp Shelby, Miss.
RUMORE, Emanuel V., 1st Lieut., Brooklyn, Air Base, Meridian, Miss.
RUSTIN, Howard F., 1st Lieut., Brooklyn, Advanced Flying School, Selma, Ala.
RYAN, David F., 1st Lieut., Yonkers, N. Y., Camp Shelby, Miss.
RYTERBAND, Louis, 1st Lieut., Brooklyn, Air Base, Jackson, Miss.
SALMERI, Edward J., 1st Lieut., Woodridge, N. J., Fort McClellan, Ala.
SALTZ, Herman P., 1st Lieut., Jersey City, N. J., Fort Jay, N. Y.
SANDFORD, Francis R., Jr., 1st Lieut., Arlington, N. J., Fort Bragg, N. C.
SARADARIAN, Albert V., 1st Lieut., Union City, N. J., Fort Jay, N. Y.
SCALISE, Salvatore, 1st Lieut., Brooklyn, Camp Lee, Va.
SCHULTZ, Elak, 1st Lieut., New York, Air Base, Savannah, Ga.
SCHAUS, James P., 1st Lieut., Buffalo, Fort Niagara, N. Y.
SCURTI, Bernard V., 1st Lieut., Canisteo, N. Y., Camp Shelby, Miss.
SEGAL, Lester, 1st Lieut., New York, Camp Shelby, Miss.
SENNÉ, Hubert S., 1st Lieut., Glendale, N. Y.; Advanced Flying School, Albany, Ga.
SHAPIRO, Edward E., 1st Lieut., Bayonne, N. J., Camp Shelby, Miss.
SHAROFF, Robert L., 1st Lieut., Brooklyn, 134th Medical Regiment, Fort Bragg, N. C.
SHEFT, Matthew J., 1st Lieut., Passaic, N. J., Plattsburg Barracks, N. Y.
SOEHNER, Bernard P., 1st Lieut., Rochester, N. Y., Fort Niagara, N. Y.
SORNBERGER, Charles F., 1st Lieut., Cortland, N. Y., Fort Ontario, N. Y.
SPAETH, Frank, 1st Lieut., Syracuse, N. Y., Pine Camp, N. Y.
STAAB, Frederick D., 1st Lieut., Rochester, N. Y., Fort Niagara, N. Y.
STAUB, Philip L., 1st Lieut., Brooklyn, Camp Stewart, Ga.
STEIN, Lester M., 1st Lieut., Brooklyn, Induction Station, Trenton, N. J.
STRAUSS, Samuel D., 1st Lieut., Albany, N. Y., Elgin Field, Valparaiso, Fla.
TERR, Isaac, 1st Lieut., Woodmere, L. I., Camp Claiborne, La.
TRAVIS, Leroy O., 1st Lieut., Great Neck, L. I., Fort Jackson, S. C.
UNGER, Paul N., 1st Lieut., Brooklyn, Air Base, Jackson, Miss.
URBANOWICZ, Stanley T., 1st Lieut., Buffalo, Fort Niagara, N. Y.
VAN BUREN, John J., 1st Lieut., Brooklyn, Air Base, Baton Rouge, La.
VAN HOV, Joe M., 1st Lieut., New York, Fort Hancock, N. J.
VOGEL, Nathan F., 1st Lieut., East Orange, N. J., Air Base, Tallahassee, Fla.
VOURNAS, Christopher G., 1st Lieut., Brooklyn, Fort Du Pont, Del.
WADRO, Harold S., 1st Lieut., New York, Air, Meridian, Miss.
WAY, Clarence W., Major, Sea Isle City, N. J., Fort Dix, N. J.
WEINSTEIN, George J., 1st Lieut., Brooklyn, Air Base, West Palm Beach, Fla.
WEISMAN, Edward, 1st Lieut., Brooklyn, Camp Shelby, Miss.
WEST, Theodore S., Major, Port Chester, N. Y., General Dispensary, New York.
WEXEBLATT, Robert, 1st Lieut., Brooklyn, Air Base, Meridian, Miss.
WEYNERT, Joseph B., 1st Lieut., Brooklyn, Fort Bragg, N. C.
WHITBECK, Carl B., 1st Lieut., Hudson, N. Y., Fort Dix, N. J.
WIGH, Russell, 1st Lieut., Jersey City, N. J., Fort Dix, N. J.
WISHIK, Julian L., 1st Lieut., Flushing, N. Y., Advanced Flying School, Selma, Ala.
WOLFSIE, Jack H., 1st Lieut., New York, Air Base, Augusta, Ga.
WOODIN, William G., 1st Lieut., Dunkirk, N. Y., Pine Camp, N. Y.
YAVELOW, Charles S., 1st Lieut., Mount Vernon, N. Y., Flying Cadet Examining Board, New York.
ZATZKIN, Herbert R., 1st Lieut., New Brunswick, N. J., Air Base, Orlando, Fla.
ZOLL, John G., 1st Lieut., Buffalo, Fort Niagara, N. Y.

Orders Revoked

ANGELO, Martin A., 1st Lieut., Buffalo.
BABBIT, Hugh M., Jr., 1st Lieut., Plainfield, N. J.
BAKER, Augustus L., 1st Lieut., Camp Shelby, Miss.
BERGSTEIN, Joseph, Captain, Brooklyn.
BOLKER, Abraham, 1st Lieut., Brooklyn.
BUMP, Samuel C., 1st Lieut., Ridgewood, N. J.
CALABRESE, Dino D., 1st Lieut., Camp Shelby, Miss.
DeHOFF, John B., 1st Lieut., Air Base, West Palm Beach, Fla.

DEIBERT, Kirk R., 1st Lieut., Woodlynne, N. J.
DOMANO, Patrick J., 1st Lieut., Orange, N. J.
DURHAM, James R., Jr., 1st Lieut., Wilmington, Del.
FEIGIN, Emanuel V. D., Captain, Lincoln, Neb.
GLENN, James A., Jr., 1st Lieut., North Creek, N. Y.
HOWLAND, Reeve S., 1st Lieut., Elmira, N. Y.
HYMAN, Aaron, 1st Lieut., New York.
JANNARONE, Lewis H., 1st Lieut., Fort Jackson, S. C.
JESURUN, Harold M., 1st Lieut., Fort Bragg, N. C.
KORKOSZ, August B., 1st Lieut., Schenectady, N. Y.
LaBARBERA, Thomas, 1st Lieut., Brooklyn.
LAMBERTI, John J., 1st Lieut., Air Base, Augusta, Ga.
LEADLEY, Jerome H., 1st Lieut., Rochester, N. Y.
LEAMAN, Granville M., 1st Lieut., East Orange, N. J.
LOVELOCK, Francis J., 1st Lieut., Fort Wadsworth, N. Y.
METCALF, Frederic U., 1st Lieut., Rockville Centre, N. Y.
NEWMAN, Ernest B., 1st Lieut., Camp Blanding, Fla.
O'TOOLE, John S., Jr., 1st Lieut., Potsdam, N. Y.
PATTI, Samuel R., 1st Lieut., Dunkirk, N. Y.
ROWE, Kenneth T., 1st Lieut., Dansville, N. Y.
SCHMIDT, Christian W., 1st Lieut., Burdett, N. Y.
SMITH, Harry G., 1st Lieut., New York.
THALER, Joseph L., 1st Lieut., Rochester, N. Y.
TIRRELL, Chester M., 1st Lieut., Newark, N. J.
VOGEL, Nathan F., 1st Lieut., Air Base, Tallahassee, Fla.
WINTER, Carl M., 1st Lieut., Camden, N. J.

SIXTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Sixth Corps Area, which comprises the states of Wisconsin, Illinois and Michigan:

BABBITZ, Sidney G., 1st Lieut., Milwaukee, 33d Division, Camp Forrest, Tenn.
BALUSS, John William, Jr., 1st Lieut., Ann Arbor, Mich., Selfridge Field, Mount Clemens, Mich.
BARRON, Elmer A., 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
BARTHOLIC, Francis W., 1st Lieut., Grass Lake, Mich., 33d Division, Camp Forrest, Tenn.
BECK, Karl H., 1st Lieut., Detroit, 33d Division, Camp Forrest, Tenn.
BEHNKE, Charles H., 1st Lieut., Wauwatosa, Wis., U. S. Army Induction Station, Kalamazoo, Mich.
BERG, George S., 1st Lieut., Chicago, 135th Medical Regiment, Camp Shelby, Miss.
BLEIER, Robert S., 1st Lieut., Chicago, 11th Station Hospital, Fort Custer, Mich.
CALOSIO, Richard T., 1st Lieut., Joliet, Ill., 27th Division, Fort McClellan, Ala.
CIGANY, Zoltan B., 1st Lieut., Waltz, Mich., 135th Medical Regiment, Camp Shelby, Miss.
CHOY, James K. L., 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
COHN, Isadore H., 1st Lieut., Chicago, 135th Medical Regiment, Camp Shelby, Miss.
CORTOPASSI, Vital E., 1st Lieut., Saginaw, Mich., 33d Division, Camp Forrest, Tenn.
CRANE, Wesley T., 1st Lieut., Northbrook, Ill., 40th Corps Area Brigade (AA), Fort Sheridan, Ill.
DICKMAN, Harry M., 1st Lieut., Detroit, 33d Division, Camp Forrest, Tenn.
ENGELMANN, Andrew T., 1st Lieut., LaCrosse, Wis., 3d Armored Division, Camp Polk, La.
FORKOSH, Sydney R., Captain, Chicago, 30th Division, Fort Jackson, S. C.
FINCH, Sinclair F., 1st Lieut., Armada, Mich., 33d Division, Camp Forrest, Tenn.
FREEMAN, Gustave, 1st Lieut., Chicago, 4th Armored Division, Pine Camp.
FRISCH, Robert A., 1st Lieut., Milwaukee, U. S. Army Induction Station, Milwaukee.
GANTZ, Hyman A., 1st Lieut., Waukesha, Wis., 33d Division, Camp Forrest, Tenn.
GENETTI, Emil J., 1st Lieut., Bessemer, Mich., 33d Division, Camp Forrest, Tenn.
GINSBERG, Julius E., 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
GOLDSTEIN, Hyman H., 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
GORDON, Louis Z., 1st Lieut., Peoria, Ill., 4th Armored Division, Pine Camp, N. Y.
GREENE, Bernard L., 1st Lieut., Elgin, Ill., 33d Division, Camp Forrest, Tenn.
GROSSMAN, William L., 1st Lieut., Manteno, Ill., 27th Division, Fort McClellan, Ala.
HEBENSTREIT, Kenneth J., 1st Lieut., Chicago, 4th Armored Division, Pine Camp, N. Y.
HENSKE, William C., Captain, Chippewa Falls, Wis., 29th Division, Fort Meade, Md.
HILKER, Albert W., 1st Lieut., Chicago, 191st Tank Battalion, General Headquarters, Reserve National Guard, Fort Meade, Md.
HILL, Edward L., 1st Lieut., Jacksonville, Ill., 135th Medical Regiment, Camp Shelby, Miss.
HOFFMAN, John M., 1st Lieut., Chicago, 29th Division, Fort Meade, Md.
HUFFMAN, Carroll W., 1st Lieut., Chicago, U. S. Army Induction Station, Detroit.
JANA, Joseph T., 1st Lieut., Berwyn, Ill., 29th Division, Fort Meade, Md.
JANSON, Carl H., 1st Lieut., Homewood, Ill., 33d Division, Camp Forrest, Tenn.
JUSTEN, Ralph T., 1st Lieut., Milwaukee, 33d Division, Camp Forrest, Tenn.
KAHN, Jack L., 1st Lieut., Chicago, 3d Armored Division, Camp Polk, La.
KAPUSTIAK, Wendell A., 1st Lieut., Chicago, 4th Armored Division, Pine Camp, N. Y.
KAREN, Robert, 1st Lieut., Milwaukee, 33d Division, Camp Forrest, Tenn.
KAUPPINEN, Jalo A., 1st Lieut., Grand Rapids, Mich., 33d Division, Camp Forrest, Tenn.
KLIEGER, Samuel, 1st Lieut., Augusta, Mont., 33d Division, Camp Forrest, Tenn.
KOZA, John L., 1st Lieut., Chicago, 135th Medical Regiment, Camp Shelby, Miss.
KUHLMANN, Raymond F., 1st Lieut., Milwaukee, 135th Medical Regiment, Camp Shelby, Miss.
LASH, Sidney R., 1st Lieut., Chicago, 1604th Corps Area Service Unit, Medical Section, Fort Brady, Mich.
LENTINI, Joseph R., 1st Lieut., Grand Rapids, Mich., 3d Armored Battalion, Camp Polk, La.
LEVAGOOD, Floyd B., 1st Lieut., Detroit, 59th Signal Battalion, Fort Knox, Ky.
LEVY, Joseph, 1st Lieut., Battle Creek, Mich., 191st Tank Battalion, General Headquarters, Reserve National Guard, Fort Meade, Md.
MALEC, John P., 1st Lieut., Madison, Wis., 33d Division, Camp Forrest, Tenn.
MALOOF, George J., 1st Lieut., Madison, Wis., 135th Medical Regiment, Camp Shelby, Miss.
MALSBURY, Charles W., 1st Lieut., Virden, Ill., 135th Medical Regiment, Camp Shelby, Miss.
MAXWELL, James H., Jr., 1st Lieut., Detroit, Station Complement, Selfridge Field, Mich.
MAYKA, John P., 1st Lieut., Chicago, 135th Medical Regiment, Camp Shelby, Miss.
MOORE, Eugene F., Captain, Collinsville, Ill., 29th Division, Fort Meade, Md.
MOSIMAN, William D., 1st Lieut., Morton, Ill., 3d Armored Division, Camp Polk, La.
NEEB, Walter G., 1st Lieut., Detroit, 135th Medical Regiment, Camp Shelby, Miss.
NEFCHES, Michael Stanley, Captain, Red Oak, Iowa, 135th Medical Regiment, Camp Shelby, Miss.
OLMSTED, Kenneth L., 1st Lieut., Coldwater, 33d Division, Camp Forrest, Tenn.
PASTRON, Seymour S., 1st Lieut., Chicago, 3d Armored Division, Camp Polk, La.
PERLMUTTER, Harold M., 1st Lieut., Chicago, 2d Armored Division, Fort Benning, Ga.
PFEFFER, Isadore S., 1st Lieut., Eloise, Mich., 33d Division, Camp Forrest, Tenn.
PERSSION, Leo B., 1st Lieut., Milwaukee, 135th Medical Regiment, Camp Shelby, Miss.
PORRITT, Ross J., 1st Lieut., Pontiac, Mich., 33d Division, Camp Forrest, Tenn.
PORTS, Preston W., Captain, Farmington, Mich., Station Complement, Selfridge Field, Mich.
REANEY, Burnell V., 1st Lieut., Chicago, 5th Station Hospital, Fort Stewart, Ga.
RETTIG, Frank E., Captain, Wauwatosa, Wis., 29th Division, Fort Meade, Md.
ROGERS, Albert F., 1st Lieut., Milwaukee, 33d Division, Camp Forrest, Tenn.
ROSEN, Benjamin B., 1st Lieut., Chicago, 135th Medical Regiment, Camp Shelby, Miss.
ROYCE, Grant E., 1st Lieut., Harvard, Ill., U. S. Army Induction Station, Milwaukee.
RUSKIN, Dave B., 1st Lieut., Wahjamega, Mich., 3d Armored Division, Camp Polk, La.
SALZMAN, Jay Marvin, Captain, Springfield, Ill., 29th Division, Fort Meade, Md.
SCHIFF, Isadore J., 1st Lieut., Chicago, Air Base, Albuquerque, N. M.
SCHWEITZER, Edmund H., 1st Lieut., Peoria, Ill., 33d Division, Camp Forrest, Tenn.
SHEMANSKI, Leonard S., 1st Lieut., Menasha, Wis., 29th Division, Fort Meade, Md.
SIEGEL, Morris, 1st Lieut., Chicago, 4th Armored Division, Pine Camp, N. Y.
SIMONS, Morton, 1st Lieut., Chicago, 33d Division, Camp Forrest, Tenn.
SLAYBAUGH, James C., Captain, Wood, Wis., Armored Force Troop Unit, Fort Benning, Ga.
SMITH, Eldon E., 1st Lieut., Wausau, Wis., 135th Medical Regiment, Camp Shelby, Miss.
SMITH, Fred Robert, 1st Lieut., Detroit, 3d Armored Division, Camp Polk, La.
SMITH, Carleton R., 1st Lieut., Villa Grove, Ill., Station Complement, Camp Croft, S. C.
STEPHEN, Robert J., 1st Lieut., Joliet, Ill., 33d Division, Camp Forrest, Tenn.
STONE, Ethon L., 1st Lieut., Detroit, 3d Armored Division, Camp Polk, La.
TEMKIN, Mark M., 1st Lieut., Beaver Dam, Wis., 33d Division, Camp Forrest, Tenn.

TEPPER, Sidney M., 1st Lieut., Chicago, Station Hospital, Fort Sill, Okla.
VACANTE, Anthony B., 1st Lieut., Chicago, 12th Station Hospital, Camp Forrest, Tenn.
WEIDNER, Morris R., 1st Lieut., Dolton, Ill., 135th Medical Regiment, Camp Shelby, Miss.
WELSH, Sylvester M., Captain, Prairie du Chien, Wis., 29th Division, Fort Meade, Md.
WERBEL, Ernest W., 1st Lieut., Chicago, 135th Medical Regiment, Camp Shelby, Miss.
WYNES, Maurice C., 1st Lieut., Saginaw, Mich., 3d Armored Division, Camp Polk, La.
YOUNG, Leslie W., 1st Lieut., Fairfield, Ill., Selfridge Field, Mount Clemens, Mich.
ZMYSLONY, Walter P., Captain, Milwaukee, 33d Division, Camp Forrest, Tenn.
ZURFLI, Clarence J., 1st Lieut., Chicago, 29th Division, Fort Meade, Md.

Orders Revoked

ALTMAN, Harrie P., 1st Lieut., Marengo, Ill.
BERRY, Leonidas H., 1st Lieut., Chicago.
CRAMER, Oliver S., 1st Lieut., Detroit, Selfridge Field, Mount Clemens, Mich.
FORKOSH, Sydney R., Captain, Chicago, 30th Division, Fort Jackson, S. C.
HOHMAN, Roy M., 1st Lieut., Chicago.
KACZKOWSKI, Joseph C., Major, Chicago, 9th Station Hospital, Fort McClellan, Ala.
KATZ, Charles, 1st Lieut., Chicago.
KAUFMAN, Lawrence W., 1st Lieut., Milwaukee.
KETTERER, Walter R., 1st Lieut., Breese, Ill.
LANE, Milton, 1st Lieut., Bay City, Mich., 27th Division, Fort McClellan, Ala.
LEAVITT, Samuel S., 1st Lieut., Orland Park, Ill.
MATEJKA, James J., Jr., 1st Lieut., Chicago.
MILLER, Donald Sidney, 1st Lieut., Chicago.
MOORE, Eugene F., Captain, Collinsville, Ill., 29th Division, Fort Meade, Md.
MULLEN, John P., 1st Lieut., Chicago.
MYERS, William H., Captain, Coal Valley, Ill.
NESBITT, William E., 1st Lieut., Alpena, Mich., Station Complement, Camp Wheeler, Ga.
OSTRANDER, Robert A., 1st Lieut., Ludington, Mich.
PARKER, Elliott F., 1st Lieut., Moline, Ill.
PISZCZEK, Edward A., 1st Lieut., Chicago.
RETTIG, Frank E., Captain, Wauwatosa, Wis., 29th Division, Fort Meade, Md.
WESCOTT, Royal J., 1st Lieut., Marquette, Mich., 11th Station Hospital, Fort Custer, Mich.
WORDEN, Robert W., 1st Lieut., Chicago, 207th General Hospital, Camp Livingston, La.
WRIGHT, Marvin, 1st Lieut., Rhinelander, Wis.

NINTH CORPS AREA

The following additional medical reserve corps officers have been ordered to extended active duty by the Commanding General, Ninth Corps Area, which comprises the states of Washington, Montana, Oregon, Nevada, Utah, California and Idaho:

ANTONINI, Charles John, 1st Lieut., San Francisco, 40th Division, Camp San Luis Obispo, Calif.
AUERBACH, Joseph, 1st Lieut., San Francisco, 40th Division, Camp San Luis Obispo, Calif.
BERKOVE, Alfred B., Captain, Oakland, Calif., Camp San Luis Obispo, Calif.
BERMAN, Harry, Captain, Ogden, Utah, Station Hospital, March Field, Calif.
BRYANT, Frank A. M., Captain, Los Angeles, Camp San Luis Obispo, Calif.
BURGER, Raymond A., 1st Lieut., West Los Angeles, Calif., 9th Army Corps, Fort Lewis, Wash.
CARLQUIST, John H., 1st Lieut., Salt Lake City, Camp Roberts, Calif.
CONLAN, Francis J., 1st Lieut., San Francisco, Camp San Luis Obispo, Calif.
CULLIMORE, Leland K., 1st Lieut., Tacoma, Wash., Camp Roberts, Calif.
EMMENS, Thomas H., 1st Lieut., Medford, Ore., Station Hospital, Fort Lewis, Wash.
FRANCIS, Horace M., Colonel, Corvallis, Ore., Station Hospital, Fort Lewis, Wash.
GANS, Paul J., 1st Lieut., Lewiston, Mont., 9th Army Corps, Fort Lewis, Wash.
GORDON, Jack D., 1st Lieut., French Camp, Calif., Camp San Luis Obispo, Calif.
HONEYCUTT, Charles F., Jr., 1st Lieut., Missoula, Mont., Camp San Luis Obispo, Calif.
JACKSON, Henry M., Captain, Salt Lake City, 9th Army Corps, Fort Lewis, Wash.
KLAUSNER, John T., Captain, Los Angeles, Hamilton Field, Calif.
LEWIS, Charles F., 1st Lieut., Oakland, Calif., Camp San Luis Obispo, Calif.
MEEHAN, Carl W., 1st Lieut., Sacramento, Calif., 9th Army Corps, Fort Lewis, Wash.
MEYER, Emerson L., 1st Lieut., Healdsburg, Calif., Camp San Luis Obispo, Calif.
MICHELS, Leon M., Captain, San Francisco, Camp San Luis Obispo, Calif.
MILLER, Clark R., 1st Lieut., San Francisco, Camp San Luis Obispo, Calif.
MORRIS, Francis B. O'N., 1st Lieut., Los Angeles, Camp San Luis Obispo, Calif.
NETHERY, Robert D., 1st Lieut., Covina, Calif., Hamilton Field, Calif.
OVSEY, Lionel, 1st Lieut., Los Angeles, Camp Haan, Riverside, Calif.
PETERFY, Richard A., Captain, Los Angeles, Camp San Luis Obispo, Calif.
POTTER, Clarence G., Captain, San Francisco, Hamilton Field, Calif.
ROBINSON, Hewitt H., Major, Oakland, Calif., Corps Area Service Command, Fort Ord, Calif.
SKEOCH, Gordon D., 1st Lieut., Los Angeles, Corps Area Service Command, 1962, Fort Ord, Calif.
STANSBURY, John R., 1st Lieut., Santa Barbara, Calif., Camp San Luis Obispo, Calif.
TUCKER, Edwin W., 1st Lieut., Visalia, Calif., Camp San Luis Obispo, Calif.
WALSH, Alton L., 1st Lieut., Portland, Ore., 203d General Hospital, Fort Lewis, Wash.
WHITELY, Edward J., 1st Lieut., Fort Baker, Calif., Camp San Luis Obispo, Calif.
YOST, Raiph E., 1st Lieut., Glendale, Calif., March Field, Calif.

Orders Revoked

COLLINS, Robert F., 1st Lieut., North Hollywood, Calif.
WASSERMAN, Sidney E., Captain, March Field, Calif.

Relieved from Duty

COULTER, James D., Captain, Fort Ord, Calif.
DALE, Earl E., Major, Fort Missoula, Mont.
KARLEEN, Philip E., Captain, Fort Ord, Calif.
PITMAN, H. T., 1st Lieut., Fort Ord, Calif.

ORDERED TO AND FROM FOREIGN DUTY

BEATY, Sam, 1st Lieut., M. R. C., U. S. Army, from Fort Sam Houston, Texas, to the Puerto Rican Department, sailing from Charleston, June 20.
BOAL, Robert W., M. C., U. S. Army; FUGELSO, Erling S., M. C., U. S. Army; KELLEY, Robert R., M. C., U. S. Army; KIND, Henry A., M. C., U. S. Army; KIRKMAN, Lewis W., M. C., U. S. Army, and RICHMOND, Albert M., M. C., U. S. Army.
BRADFORD, Aubrey L., Major, M. C., U. S. Army, from Washington, D. C., to the Panama Canal Department, sailing from New York, July 17.
BROWNING, John R., 1st Lieut., M. R. C., U. S. Army, from Camp Upton, N. Y., to the Hawaiian Department, sailing from New York, June 26.
COCKERHAM, Howard L., Jr., 1st Lieut., M. R. C., U. S. Army, Fort Belvoir, Va., to the Hawaiian Department, sailing from New York, June 26.
EVANS, Charles W., Jr., 1st Lieut., M. R. C., U. S. Army, from El Paso, Texas, to the Puerto Rican Department, sailing from Charleston, S. C., June 20.
FENTON, Bryan C. T., Captain, M. C., U. S. Army, from Hawaiian Department to the Office of the Surgeon General, Washington, D. C.
FREED, Albert E., 1st Lieut., M. R. C., U. S. Army, from Fort Leavenworth, Kan., to the Hawaiian Department, sailing from New York, June 26.
GARRETT, Robert T., 1st Lieut., M. R. C., U. S. Army, from Washington, D. C., to the Hawaiian Department, sailing from San Francisco, July 16.
GRIGSBY, Kenneth R., Captain, M. R. C., U. S. Army, from Fort Crook, Neb., to the Panama Canal Department, sailing from New York, June 26.
HENDRICKSON, Harvey F., Major, M. C., U. S. Army, from Panama Canal Department to Port of Embarkation, Brooklyn.
HOUSE, Rex, Captain, M. C., U. S. Army, from Washington, D. C., to the Panama Canal Department, sailing from New York, June 26.
JOHANNES, Henry C., Lieut. Colonel, M. C., U. S. Army, from Hawaiian Department to San Francisco Port of Embarkation, Fort Mason, Calif.
KING, John H., Jr., Captain, M. C., U. S. Army, from Philippine Department to Army Medical Center, Washington.
MILHOLLAND, Arthur V., 1st Lieut., M. R. C., U. S. Army, from Fort Belvoir, Va., to the Hawaiian Department, sailing from New York, June 26.
NOE, Joe T., Jr., 1st Lieut., M. R. C., U. S. Army, from Fort Knox, Ky., to the Panama Canal Department, sailing from New York, June 26.

POWER, William J., Captain, M. C., U. S. Army, from Panama Canal Department to Port of Embarkation, Brooklyn.

RAMSAY, Lewis C., 1st Lieut., M. R. C., U. S. Army, from Fort McClellan, Ala., to the Hawaiian Department, sailing from Charleston, S. C., June 28.

RICHARDSON, Frank L., M. R. C., U. S. Army, from Fort Ord, Calif., to the Philippine Department, sailing from San Francisco, June 5.

RIZZOLO, John, 1st Lieut., from Aberdeen Proving Ground, Md., to the Philippine Department, sailing from San Francisco, July 17.

SMITH, Wilson T., Captain, M. C., U. S. Army, from Hawaiian Department to Letterman General Hospital, San Francisco.

TONEY, William E., 1st Lieut., M. R. C., U. S. Army, from Camp Joseph T. Robinson, Ark., to the Hawaiian Department, sailing from Charleston, June 28.

VADALA, Anthony J., Lieut. Colonel, M. C., U. S. Army, from Panama Canal Department to Port of Embarkation, Brooklyn.

WILLIAMS, Martin P., Captain, M. R. C., U. S. Army, from Fort Knox, Ky., to the Hawaiian Department, sailing from New York, June 26.

MEDICAL FINDINGS OF INDUCTION BOARDS IN NEW YORK CITY

A report submitted by Col. Samuel J. Kopetzky, chief of the Medical Division of the New York City Selective Service Administration, covering the first fourteen induction periods up to June 30, 1941, shows that 115,569 registrants were examined, of whom 42.8 per cent classified on the basis of their physical examination were inducted into the army; 30.26 per cent were qualified for limited military service only and 26.85 per cent were disqualified for any military service. Of the 34,977 registrants qualified by the board for limited military service, 28,163 registrants had only one physical defect and 21,367 of the 31,025 registrants disqualified for any military service had only one defect. It would seem likely, therefore, that a much greater number of the men could be treated and made available for service under class 1-A than for 1-B. A prehabilitation program, therefore, has been set in motion whereby the practical means to arrange for the treatment of registrants will be available, Col. Arthur McDermott, New York City Selective Service director, said. A medical social worker will be attached to each local board and, with the registrant's consent and the recommendation of the examining physician, will make arrangements for the registrant to receive treatment either from a private physician or, if he cannot afford to pay, at a clinic. Thus many of the men now medically unfit for military service can be treated so they will qualify for limited service at least. Colonel McDermott added that the future usefulness of these young men to themselves and to society and the health of the nation are as much involved as national defense. However, a man may have only one defect which may not be remediable and a man may have more than one defect and each one of them may be remediable and be cured. Among the defects easily remedied so that those having one or more could be put into condition for class 1-A are hernia, varicocele, gonorrhea, syphilis, infected gums and the replacing of extracted teeth with bridges.

The most frequent causes for qualifying a registrant for limited military service are defects of the eyes and teeth, 10.39 per cent and 9.39 per cent respectively, defects of the extremities 4.19 per cent, of the genitourinary organs and venereal disease 3.63 per cent, and abdominal organs and abdominal wall 3.56 per cent.

The most frequent reasons for disqualifying a registrant for military service (class IV-F) were defects of the heart and blood vessels 10.61 per cent, defects of the extremities 4.04 per cent, mental and nervous disorders 4.98 per cent, and defects of the ears 3.39 per cent, of the eyes 3.13 per cent, of the teeth 2.13 per cent and of the lungs 2.10 per cent.

This report, which was prepared under the supervision of Dr. Arthur M. Tiber, throws light on the health of New York City registrants as affected by tuberculosis, syphilis and psychiatric disorders. A special study of pulmonary tuberculosis among an unselected group of registrants from local Board 1 (lower Broadway, Chinatown and part of Mulberry Street) made by roentgen ray examination showed that of 1,090 men examined 8.7 per cent had pulmonary tuberculosis, which disqualified them for any military service. Colonel Kopetzky pointed out that Local Board 1, while typical of the city as far as the percentage of men accepted for full military training goes, has a higher percentage of those medically unfit for any kind of service than any other board in the city. Local Board 1 cannot, therefore, be considered typical of the registrants as a whole as regards pulmonary tuberculosis. However, used as a basis for estimation, about 6.5 per cent of all New York City registrants between 21 and 36 would have pulmonary tuberculosis to an extent that would disqualify them for service.

The syphilis picture for New York City is encouraging, as only 1.65 per cent of the 115,569 registrants examined had two positive serologic tests for syphilis, and of these 1,687 were qualified for limited military service and only 216 disqualified for any military service.

Every registrant sent to the induction station has a psychiatric examination there. At the local boards, however, only those receive a psychiatric examination who in the opinion of the examining physicians need it. According to this report, only 233 registrants were placed in class 1-B because of mental and nervous disorders of a mild character, while 5,759 were disqualified for any kind of military service on account of severe mental and nervous disorders.

This statistical report is based solely on the record put on form D. S. S. 200 and is concerned only with the final physical classification into which the registrant has been placed. When a registrant is rejected at the induction examination and he has a temporary illness, his D. S. S. form 200 is held at the local board until he recovers. Later, after again being examined at the induction station, he is often accepted.

During the period under survey by this report, an experimental preinduction examination station was functioning in this area. This station was established to determine the practicability of having a preinduction medical examination to provide the registrant with more time to settle his individual affairs if he passed the physical test, and to obviate the necessity of returning him to civil life because he was rejected after he had made all arrangements to enter the army. This plan has worked well. In addition to the registrants previously cited, 3,583 were examined and accepted for full military duty at the preinduction station and are now waiting induction when the local time interval shall have elapsed before going directly into service.

CCC CAMPS

The appropriation approved by Congress for the current fiscal year provides for the maintenance of one thousand, two hundred and thirty-six CCC camps throughout the country and an average total enrolment of two hundred and thirty-two thousand, five hundred enrolees. The strength of the CCC on July 20 was about one hundred and ninety thousand, but it is estimated that four hundred and fifty thousand young men and war veterans will receive training useful in national defense during the current fiscal year. Of the one thousand, two hundred and thirty-six camps, about one hundred will be assigned to work on military reservations, army hospitals and so on to expand the facilities for the enlarged army. Seven hundred and ninety-three camps have been assigned to work supervised by the Department of Agriculture, and three hundred and eighty-six camps to work supervised by the Department of the Interior. Twelve New England camps are scheduled for closing after August 1. One of the major types of work to be carried on will be the protection of timber areas, including forest fire fighting, fire hazard reduction, the construction of truck trails, telephone lines, fire breaks and lookout towers and erosion control. During September they will begin the planting of trees, grasses and shrubs and the development of recreational areas in forests and parks and of refuges for wild life.

The CCC training program will center around courses useful in national defense and after-work classes will be conducted in every camp. There will be one hundred and seventy-six

special CCC schools and shops for training in radio operation, automobile mechanics, cooks and call clerks, while other national defense courses will be given to about forty thousand enrolees in cooperation with neighboring vocational schools.

EXAMINATION FOR APPOINTMENTS IN THE NAVY

An examination will be held at all of the larger naval hospitals and at the Naval Medical Center, Washington, D. C., for appointments as acting assistant surgeon for intern training and as assistant surgeon. For the former position, examinations will be held Oct. 6-9, 1941 and Jan. 5-9, 1942 and for the latter Aug. 11-15, 1941, Oct. 6-9, 1941 and Jan. 5-9, 1942. Applications for authorization to take the examination must be in the Bureau of Medicine and Surgery, Navy Department, Washington, D. C., three weeks prior to the examination. The bureau will forward application forms on request and, in addition, a circular of information for applicants listing details concerning physical requirements, professional examination, rates of pay, and promotion and retirement data. Applicants for appointment as acting assistant surgeon for intern training are required to be citizens of the United States of over 21 but less than 32 years of age, members of the junior or senior classes in class A approved medical schools and to meet the physical and other requirements for appointment. For appointment as assistant surgeon applicants are required to be citizens of the United States of over 21 but less than 32 years of age, graduates of approved medical schools, to have had at least one year of intern training in a hospital accredited for intern training by the Council on Medical Education and Hospitals of the American Medical Association and to meet the physical and other requirements.

MISS BARBER APPOINTED FOOD CONSULTANT

Miss Mary I. Barber, Battle Creek, Mich., president of the American Dietetic Association, has returned to the War Department as food consultant to the Secretary of War and has been assigned to the subsistence branch of the Quartermaster Corps. Last winter she was an appointee of the Office of Production Management, assigned to the Quartermaster Corps. Miss Barber will assist with menus to see that men in military camps are getting both a tasty and a well balanced diet and will give talks before various agencies throughout the country. According to the Bureau of Public Relations of the War Department, more than a hundred members of the American Dietetic Association are employed in army hospitals; one has gone overseas with the Harvard medical units and a hundred and ninety-four are enrolled with the American Red Cross, forming a reserve which the army can call on in case of emergency.

MORE RECREATIONAL AREAS

Six more recreational areas were authorized for construction, the War Department announced July 16. The location of the new camps and their week end capacities are: Los Angeles one thousand, Fort Worth, Texas, five hundred, Oklahoma City five hundred, Kansas City, Mo., one thousand, Island Beach, N. J., five hundred and Lake Brownwood, Texas, one thousand. The week end camps are established to give soldiers free recreation facilities while on leave from their regular stations and the only cost to them is for food, which is available also at a nominal figure. Seven recreational camps are already in full operation along the gulf of Mexico, and work on fifteen others is being rushed. The new recreational camp near Washington, D. C., which will accommodate one thousand men over the week end, was dedicated on July 26. This camp is across the Potomac and north of the western approach to the Arlington Memorial Bridge, within walking distance to the Washington downtown district and affording views of the Lincoln memorial, Washington monument and the capitol dome, and yet it is located away from the dense traffic areas. The recreation camps are of permanent tent type construction, all camps being floored, framed and screened.

INTENSIFIED PROGRAM TO RECRUIT NURSES

At a conference in Washington about three weeks ago, the principal nursing groups working on national defense—National Committee on Red Cross Nursing Service, Nursing Council on National Defense and the Subcommittee on Nursing of the Health and Medical Committee of the Federal Security Agency—outlined an intensified program of nursing recruitment and of mobilizing the country's nursing strength during the present emergency. Congress recently appropriated $1,200,000 for training nurses for national defense. This fund will be used for increasing the number of students in basic nursing education programs, in preparing inactive graduate nurses for active duty and in offering postgraduate instruction in special fields of nursing. These funds are being administered by the U. S. Public Health Service, which has sent letters to all accredited schools of nursing to learn how each school may help in expanding the nation's nursing strength. Those plans submitted by various institutions which provide for the most effective and economical increase in qualified nurses will be given preference. Thomas Parran, Surgeon General of the U. S. Public Health Service, requested the appointment of three prominent nursing administrators now associated with civilian institutions to assist in the administration of the program.

THE DENTAL CORPS RESERVE

Before the present emergency there were two hundred and sixty-eight officers in the dental corps of the army and about four thousand dentists on the roll of the Dental Reserve Corps, of whom about two thousand, the War Department announced July 20, have been called to active duty. About one hundred and fifty dentists have been inducted into the army under the Selective Service and Training Act, and nearly all of them have made application for commissions. The first dentist to rise from the ranks under a new regulation permitting qualified trainees to accept commissions in the Dental Corps Reserve and to be ordered to active duty is Private Milton P. Paperth, a dentist from New Jersey now on duty at the Station Hospital, Fort Dix, N. J. Each of the one hundred and fifty dentists inducted into the army and who have now applied for commissions will be passed on by an army medical examining board and if approved will be appointed a First Lieutenant in the Dental Reserve Corps. Because the new regulation is designed to provide commissions for all qualified inducted dentists, for the present no more civilian dentists will be taken into the Dental Corps Reserve.

THE INTENSIFIED MOSQUITO CAMPAIGN

An intensified effort is getting under way to eradicate mosquitoes in and near the training centers throughout the United States and its possessions. There are fifty-three troop centers having more than ten thousand men each, and to carry out the antimosquito campaign successfully it is estimated that $250,000 a month will be required. In the 1942 army appropriation bill $1,192,000 will be appropriated for this work, and of this amount $442,000 will be turned over to the medical department and $750,000 to the quartermaster department, which will perform the patrol work under the supervision of the medical department. Eighty-seven sanitary engineers, all eradication experts, have been assigned to the camps to supervise this work, all of which will be done by civilian specialists and laborers. Soldiers will not be used for this work.

MEDICAL BOARD FOR CIVILIAN DEFENSE

A medical board to devise uniform procedure for protection of civilians in an emergency was recently appointed by the Office of Civilian Defense with the following members: Drs. Elliott C. Cutler, Boston; George Baehr, New York; Oliver B. Kiel, Wichita Falls, Texas, and Albert S. McCown, Washington, D. C.

ORGANIZATION SECTION

COURTS AND THE UNIONIZATION OF HOSPITAL EMPLOYEES

PREPARED BY THOMAS V. McDAVITT, BUREAU OF LEGAL MEDICINE AND LEGISLATION, AMERICAN MEDICAL ASSOCIATION, CHICAGO

The administrative personnel and governing boards of nongovernmental hospitals are increasingly concerned with the possibility of being confronted with demands in connection with the attempted unionization of the maintenance and other nonprofessional employees of their hospitals, and with their legal right to resist such activities. Since most private, nongovernmental hospitals depend on public donations or endowments to continue operations, and since it is practically impossible under present conditions to obtain increased donations or endowments from the public, the enforcement of demands concomitant with unionization, which almost inevitably increases operating expenses substantially, may well render affected hospitals less able to carry on their essential functions and result in a diminution in the quantity and quality of hospital services.

These so-called unionization demands stem essentially from the enactment in eight states [1] since 1937 of state labor relations acts,[2] sometimes referred to as little Wagner acts since they are patterned on the Wagner National Labor Relations Act.[3] Generally speaking, these acts create a state agency, generally referred to as a state labor relations board, with specified powers to prevent designated "unfair labor practices," one of which invariably is a refusal by an employer to bargain collectively with employees or with a union selected by the employees as their bargaining agency. Generally by these acts if a particular employer refuses to bargain collectively with his employees or perpetrates any other stated "unfair labor practice," the employees, or persons or agencies purporting to act for them, may appeal to the state labor relations board, which may order an employer to cease from carrying on the "unfair labor practices" complained of and may obtain the aid of courts in the enforcement of its order. The effect of these laws, then, is to require an employer to do certain acts in connection with his relations with his employees, which without the existence of the laws in question he could not be compelled legally to perform.

Another factor tending toward the assertion of labor demands in this connection is the enactment also in recent years of so-called labor anti-injunction acts in about twenty-five states, the general effect of which is to limit the right of state courts, or to hamper such courts, in granting injunctions in cases involving labor disputes.

Physicians and hospital boards and administrators have generally assumed that these laws have no application to a hospital, relying on an understanding or belief that these statutes deal primarily with labor disputes in industry and that a hospital is not an industry in any proper sense of the word. Recent court decisions (abstracts of three of which appear in this week's issue of THE JOURNAL) cast considerable doubt on the soundness of such an assumption. The problems involved merit thoughtful consideration and analysis.

State courts of appellate jurisdiction have considered to date 4 cases involving the applicability of state labor relations acts and labor anti-injunction acts to what essentially were attempts to press the unionization of maintenance and nonprofessional employees of hospitals and the resistance of the hospitals concerned to the unionization activities involved. It may be impossible, because of the variance in the phraseology of the applicable laws of the states in which the cases arose, to formulate accurately from an analysis of those cases and the applicable statutes any general statement that will anticipate court holdings in other states having similar laws. At any rate a discussion of the issues involved in each case would seem timely.

The first instance in which a court of appellate jurisdiction passed on the legal right of a hospital to resist unionization activities occurred in December 1937 when the supreme court, appellate division, second department, New York, in *Jewish Hospital of Brooklyn* v. *Doe,* 300 N. Y. S. 1111; J. A. M. A. **111:** 475 (July 30) 1938, held that the New York labor anti-injunction act, which limited the right of a state court to issue injunctions in labor disputes, did not prohibit the issue of an injunction asked by a charitable hospital to restrain a local union and its members, allegedly composed in part of 10 per cent of the maintenance and nonprofessional employees of the hospital, from engaging in certain activities in connection with attempts at unionization, such as disorderly mass picketing, intimidation, sit down activities and assaulting employees who refused to join the union. The court said:

> We believe, even though the statute does not expressly exempt charitable corporations, that the Legislature never intended it to apply to an institution such as plaintiff [Jewish Hospital of Brooklyn]. While those involved in a labor dispute, as defined by the statute, need not stand in the relation of employer and employee, they must be engaged in the same "industry, trade, craft or occupation." These words connote and emphasize one common thought, to wit, that the parties to the controversy shall be engaged in the same business enterprise or commercial pursuit; one motivated by the desire for profit, the other by the desire to earn a livelihood. . . . Obviously plaintiff is not engaged in any industry, trade, craft, or occupation for profit within the meaning of the statute.

But before we conclude that this case is authority for the proposition that a charitable hospital is immune from the provisions of a labor anti-injunction act or a state labor relations act, the case must be evaluated with these additional factors in mind:

1. The New York anti-injunction and labor relations acts were held to be in pari materia—that is, to be read as one and construed together—and the state labor relations act—different in this respect than any other state labor relations

1. Massachusetts, Michigan, Minnesota, New York, Pennsylvania, Rhode Island, Utah, Wisconsin.
2. Somewhat similar to these acts is also a "Labor Mediation Act" in New Jersey, which, however, lays a primary stress on arbitration alone.
3. The National Labor Relations Act applies also to the District of Columbia.

act—contains a specific exemption in favor of a charitable association, corporation or enterprise.

2. The charitable hospital in this case, it was held, discharged in part, at least, a function which ordinarily devolves on the government in that at a loss it cared for certain patients sent to it for treatment by the city and with respect to whom the city was bound to provide care. It seemed admitted that public policy at least excluded the state and its political subdivisions from the operation of the statutes involved.

A careful reading of the case then indicates that in New York the two statutes concerned would not apply probably to a nonprofit corporation, since the statutes essentially apply only where the employer is "motivated by the desire for profit." Certainly there would be no application where in addition the nonprofit corporation is performing in part a governmental function. Obviously, then, there would seem to be no exception with respect to a private hospital operated for profit and the two acts (the labor relations act and the anti-injunction act) would apply to such a hospital. That is precisely what was held on April 14, 1941 by the supreme court, appellate division, second department in *State Labor Relations Board* v. *McChesney*, 27 N. Y. S. (2d) 870 (abstracted this issue of THE JOURNAL, p. 473). The court in that case held that the New York labor relations act applies to "labor conditions in any field of employment where the objective is the earning of a livelihood on one side and the gaining of a profit on the other," and that a private hospital operated for profit was subject to the act and must comply with an order of the State Labor Relations Board requiring it to cease refusing to bargain collectively with its employees.

Next, the Supreme Court of Pennsylvania, Jan. 6, 1941, in *Western Pennsylvania Hospital et al.* v. *Lichliter*, 17 A. (2d) 206 (abstracted in this issue on page 475 and commented on editorially in THE JOURNAL Jan. 18 and June 21, 1941) upheld the action of a trial court in enjoining the Pennsylvania Labor Relations Board and a certain union from exercising jurisdiction and asserting rights, respectively, under the Pennsylvania state labor relations act in an attempt to unionize maintenance and nonprofessional employees of some twenty-five nonprofit, charitable hospitals. The Pennsylvania act, unlike the New York labor relations act, contains no express exemption in favor of charitable corporations and the reasoning employed by the court in arriving at a conclusion that the state labor relations and labor anti-injunction acts did not apply to the plaintiff hospitals is most significant. The labor anti-injunction act, the court held, did not apply since a labor dispute, within the meaning of that act, was not involved because under the act "A case shall be held to involve or to grow out of a labor dispute when the case involves persons who are engaged in a single industry, trade, craft, or occupation . . ." and, in the words of the court:

> A hospital is not an industry. Neither are the employees of a hospital engaged in a single trade, craft or occupation. Student nurses, interns, doctors, surgeons, clerks, stenographers, bookkeepers, elevator operators, ambulance drivers, laundresses, mechanics, technicians, char-women and others may be employed by a hospital. They may have a common employer but they have no single trade, craft or occupation. Giving the words "industry, trade, craft or occupation" their commonly accepted meaning, we feel that they do not include the operations of a hospital.

The court then held that, even if the words of the Pennsylvania labor relations act were interpreted as broad enough to include the operations of a hospital, still the act would have no application since, following the holding of the United States Supreme Court in *Holy Trinity Church* v. *United States*, 143 U. S. 457, 12 S. Ct. 511, a thing may be within the letter of a statute and yet not within the statute because not within its spirit. In this connection the court said:

> Hospitals are scientific institutions created for a humane purpose in amelioration of the sufferings of mankind. They require for their successful operation highly skilled physicians, surgeons, technicians, experts and nurses. They likewise require the services of other persons, some of whom may be skilled and some unskilled. But the whole must be coordinated, controlled and uninterrupted to accomplish the general purpose. This would be impossible, should we hold the Labor Act applicable with all its attending ramifications, interruptions and possible cessation of service due to labor disputes and attending financial inability to function. Surely the Legislature had no such intention and we cannot so find in the absence of a clear and positive declaration to that effect.

Moreover, most of the hospitals involved in the Pennsylvania case, the court held, were, as in the Jewish Hospital of Brooklyn case, engaged in a governmental function in that they cared for persons for whom the state had an obligation to care and received from the state appropriations which only in part reimbursed them for the costs of the services rendered to those patients. In so doing, they were governmental agencies and were exempt from the provisions of the two acts in question.

It is difficult, if not impossible, to evaluate the weight to be given to the presence of the factor of governmental agency present in this case. Without the presence of that factor and in view of the reasoning involved in the argument that the hospitals were not within the act because not within the intent of the legislature in enacting the labor relations act, a plausible argument in favor of the exemption even of private hospitals operated for profit in Pennsylvania might be convincingly advanced and possibly still can be. At least, however, it would seem to follow from the decision that in the future the Pennsylvania Supreme Court will regard a nonprofit charitable hospital, even though it does not carry on any governmental function (and it will be noted that a few of the hospitals involved in the Pennsylvania case carried on no governmental function), as exempt from the provisions of the Pennsylvania labor relations act and the Pennsylvania anti-injunction act.

The Pennsylvania case would seem to indicate that the court of another state having a state labor relations act or a similar anti-injunction act should in all logic reason likewise and accord exemption to a nonprofit charitable hospital. However, much as the logic of such a conclusion would strike one, the fact remains that the Supreme Court of Minnesota on Oct. 11, 1940 in *Northwestern Hospital, Minneapolis, Minn.* v. *Public Building Service Employes' Union Local No. 113 et al.*, 294 N. W. 215 (abstracted in this issue on page 474) rejected the argument and holding of the Pennsylvania case and squarely held that the Minnesota labor relations act applied to a labor dispute between an admittedly nonprofit, charitable hospital and its employees. In arriving at this conclusion the Minnesota court said:

> The logical starting point for an examination is with the definitions of employer and employee in the Labor Relations Act.

3. Mason Minn. St. 1940 Supp. Sec. 4254-21, provides,

> "(b) 'Employer' includes all persons employing others . . . but does not include the state or any political or governmental subdivision thereof, nor any person subject to the Federal Railway Labor Act, . . .

"(c) 'Employee' includes, in addition to the accepted definition of the word, any employee whose work has ceased because of any unfair labor practice . . . but does not include any individual employed in agricultural labor or by his parent or spouse or in domestic service of any person at his own home."

There cannot be doubt that both definitions are comprehensive in substantive nature, in fact, so much so that they force the conclusion that a nonprofit, charitable corporation operating a hospital is within the act as one "employing others." Equally certain is the proposition that one employed as an elevator operator, as a janitor or in a similar occupation is an "employee" within the accepted meaning of that term.

It may well be, however, that still other state courts would follow the Pennsylvania decision rather than the Minnesota because the Minnesota decision may possibly be justified and distinguished by particular language in the Minnesota labor relations act, which seems practically unique in this respect, providing—

If the dispute is in any industry, business or *institution* affected with a public interest, which includes, but is not restricted to, any industry, business or *institution* engaged in supplying the necessities of life, safety, or health, so that a temporary suspension of its operation would endanger the life, safety, health or well being of a substantial number of people of any community . . .

a committee appointed by the governor should hold a hearing and report on the matter. The Minnesota court placed great stress, as well it might, on the inclusion of *"institution,"* saying:

Since a state institution is within the exemption of the act, we must understand this word to mean what is commonly conveyed by it. A hospital such as plaintiff corporation operates is generally regarded as an institution in the community. It is not a business or industry but it is concerned with the well-being of the people. The intention of the legislature is more evident when consideration is given to the provision relating to the suspension of activity being a peril to a substantial number of people. It seems very apparent that just such a situation as is now before us was contemplated by this statute. There is a clear recognition that hospitals are within the act.

The presence, then, of the word "institution" would seem practically to have prohibited the Minnesota court from reading an implied exception in favor of nonprofit charitable hospitals, since the legislative intent as to inclusion seemed so evident. It may well be then that, if a particular state labor relations act does not contain any such similar language, the court construing it may be more impressed with the logic of the Pennsylvania court's holding and disregard the Minnesota holding.

In any event, while the situation with respect to nonprofit charitable hospitals in Minnesota, New York and Pennsylvania seems reasonably clear, how the courts of the other five states and the District of Columbia having labor relations acts would hold with respect to the applicability of those acts to nonprofit charitable hospitals is a matter of some conjecture based, possibly, to borrow a phrase current a few years ago, on the "economic predilections" of each particular court. The situation with respect to private hospitals conducted for profit in those states seems somewhat clearer. In principle, private hospitals conducted for profit would seem to be amenable to the labor relations act of the particular state, excepting possibly in Pennsylvania, where a logical extension of the language of the court might call for exemption.

OFFICIAL NOTES

DR. SIDWELL APPOINTED DIRECTOR OF THE CHEMICAL LABORATORY

Albert Edwin Sidwell Jr., Ph.D., has been named Director of the Chemical Laboratory of the American Medical Association. In 1931 Dr. Sidwell was graduated from Brown University, Providence, R. I., with the degree of Bachelor of Science in Chemistry. He received further training in chemistry at the University of Chicago, leading to the degree of Doctor of Philosophy in 1934. He served as assistant in chemistry at Brown University from 1928 to 1931. At the University of Chicago he held appointments as research assistant, research associate and instructor in chemistry. Dr. Sidwell has been a chemist in the Chemical Laboratory of the American Medical Association since 1938.

Dr. Sidwell has made contributions to the chemical literature in photoelectric spectrophotometry, the chemistry of hemoglobin and other pigments, and oxidation reduction problems. Dr. Sidwell is a member of the honorary society of Sigma Xi, the American Chemical Society and the Chicago Chemists' Club.

The Chemical Laboratory is a unit of the Division of Drugs, Foods and Physical Therapy of the American Medical Association.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Changes in Status.—H. R. 3484 has passed the House and is now pending in the Senate with a favorable committee report, providing that army reserve officers who were called or ordered into active military service by the federal government for service in excess of thirty days on or subsequent to Feb. 28, 1925 other than for service with the Civilian Conservation Corps, and who are now disabled from disease or injury contracted or received in line of duty while so employed, shall be entitled to receive the same retirement pay and hospital benefits as are now or may hereafter be provided by law or regulation for officers of corresponding grades and length of service of the regular army. H. R. 5146 has passed the House and is pending in the Senate with a favorable committee report, proposing to authorize an additional appropriation for the purchase of a site on which to construct a new building for the Army Medical Library and Museum.

Bills Introduced.—H. R. 5445, introduced by Representative Angell, Oregon, proposes to provide certain pensions for all persons who served ninety days in foreign service under the jurisdiction of the Quartermaster General, Surgeon General of the Army, the Secretary of the Navy or Marine Corps, during the Spanish-American War, including the Philippine Insurrection and the Chinese Boxer Rebellion. H. R. 5459, introduced by Representative Lanham, Texas, provides that seeing eye dogs or other guide dogs, specially trained and educated for that purpose, accompanied by their blind masters, shall be admitted to any building or other property owned and controlled by the United States on the same terms and conditions and subject to the same regulations as generally govern the admission of the public to such property.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

New Director of Industrial Hygiene.—Dr. Edwin H. Place, a member of the staff of the division of industrial hygiene, National Institute of Health, Bethesda, Md., has been appointed director of the division of industrial hygiene of the Alabama State Department of Health, it is reported. He succeeds Dr. John R. Cain, Montgomery, who resigned several months ago. Dr. Place graduated at Detroit College of Medicine and Surgery in 1932 and has served as director of the Des Moines County health department in Iowa and in Midland and Dickinson counties in Michigan.

CALIFORNIA

Personal.—Harold E. Jones, Ph.D., director of the Institute of Child Welfare on the Berkeley campus of the University of California, has been appointed a member of the National Research Council in the division of anthropology and psychology.

Plague Infection.—According to *Public Health Reports*, plague infection has been proved by animal inoculation and cultures in a pool of 138 fleas from 8 ground squirrels, Citellus beecheyi, received from a ranch south of Davis Ranger Station, Kern County. Plague infection was also proved in organs from a ground squirrel, Citellus beecheyi, received from about the same locality.

Criteria Indicating Death.—The San Francisco City Department of Health announces that, after a conference between the chief surgeon of the Emergency Hospital Service and the coroner, criteria indicating death have been accepted. In the future the following signs are to be looked for and checked carefully in every case of death in the institutions of the department of public health. It is mandatory that these signs be checked completely in every instance in which a patient is pronounced dead.

1. Cessation of respiration as determined by:
   (*a*) The stethoscope against the larynx.
   (*b*) Holding a mirror in front of the nose to note condensation of moisture.
   (*c*) Movement of air currents against wisps of cotton placed in the nose.
2. Cessation of heart beat as indicated by testing with the use of a stethoscope placed on the precordium.
3. Cessation of circulation as evidenced by:
   (*a*) Opacity of the hands when held up to a bright light.
   (*b*) Failure of a bleb to appear on the skin after direct application of burning heat.
   (*c*) Lividity and dependent discoloration.
4. Loss of body heat.
5. Rigor mortis.
6. Coarsening of the texture of the conjunctiva (this is not a perfectly reliable sign and neither is the state of the pupil).
7. Body decomposition.

ILLINOIS

Personal.—Dr. Thomas J. Hilliard, Fairfield, was guest of honor at a dinner, July 6, to mark his completion of fifty years in the practice of medicine. He was presented with the certificate and lapel button showing membership in the "fifty year club" of the state medical society. Dr. Leslie W. Young, Fairfield, president of the Wayne County Medical Society, was master of ceremonies.——Dr. Leon J. May, Anna, has been appointed managing officer of the Anna State Hospital, it is reported.

Respirator and Splints Available for Infantile Paralysis Cases.—The Advisory Committee of Physicians to the Cook County chapter of the National Foundation for Infantile Paralysis has notified physicians in Cook County that the chapter has available in its office at 166 West Jackson Boulevard, Chicago (telephone Wabash 8782) a supply of splints which can be obtained on request for use on any infantile paralysis patient regardless of the financial status. If the patient is able to pay for the use of the splints, this will be acceptable but it is not required. The foundation also has purchased two large respirators which are at the call of physicians of Cook County should respiratory paralysis in any patient require the use of such apparatus. Detailed information can be obtained by calling the office of the foundation.

Chicago

Special Society Elections.—New officers of the Chicago Gynecological Society include Drs. Charles E. Galloway, Evanston, president; Edward D. Allen, president-elect; William J. Dieckmann, vice president; Ralph A. Reis, treasurer, and James A. Gough, secretary.——Dr. Andrew C. Ivy was recently elected president of the Chicago Society of Internal Medicine; Dr. Harold C. Lueth, Evanston, vice president, and Dr. Richard B. Capps, secretary-treasurer.

University News.—The University of Illinois has accepted a grant of $2,000 from Parke, Davis & Company, Detroit, toward the support, for the next six months, of research on the pathogenesis and therapy of experimental renal hypertension being conducted in the departments of physiology and physiologic chemistry of the college of medicine by Dr. George E. Wakerlin and Carl A. Johnson, Ph.D. A paper by these authors appears on p. 416 in this issue of THE JOURNAL.

Maternal and Infant Mortality.—Maternal mortality reached the low point of twenty-four deaths per 10,000 live births in Chicago in 1940, according to an announcement from the Joint Maternal Welfare Committee of Cook County. The infant mortality under 1 year of age was 28.8 per thousand live births in 1940, a reduction from the rate of 31.3 for 1939. A noteworthy reduction in the mortality of infants under 1 day of age has occurred, from 15.5 per thousand live births in 1935 to 10.9 in 1940. The stillbirth rate has been reduced from 26.9 per thousand live births in 1935 to 25.4 per thousand live births in 1940.

KENTUCKY

Society News.—The Trigg County Medical Society was organized in Cadiz, July 22, with Drs. George E. Hatcher, Cerulean, as president and Elias Futrell, Cadiz, secretary.——At a meeting of the Tri-County Medical Association composed of Hickman, Carlisle and Ballard counties in Wickliffe in June the speakers were Drs. John F. Dunn, Arlington, on treatment of fractures and Horace E. Titsworth, Clinton, on gastric syphilis.

Dr. Rankin Honored.—The Fayette County Medical Society gave a banquet at the Lexington Country Club, June 30, in honor of Dr. Fred W. Rankin, Lexington, recently named President-Elect of the American Medical Association. Dr. Charles M. McKinlay, Lexington, president of the county society, presided and guests included Drs. Harrison H. Shoulders, Nashville, Tenn., Speaker of the House of Delegates; Elmer L. Henderson, Trustee; Irvin Abell, Past President; James Duffy Hancock, member of the House of Delegates of the American Medical Association, and Arthur T. McCormack, state health commissioner and also a delegate, all of Louisville.

LOUISIANA

Federal Funds for Research.—Tulane University of Louisiana School of Medicine, New Orleans, will receive federal funds to carry on research in the field of malaria control and Charity Hospital, New Orleans, for research in the use of sulfanilamide compounds in treating infections resulting from wounds and burns, newspapers reported. Funds will also be allotted to Tulane for work on malaria control and mosquito control and for the study of roentgen therapy in gas gangrene.

Group to Coordinate Health Actjvities.—The Louisiana State Council for the Coordination of Health, Welfare and Recreational Activities in National Defense was organized in the offices of Welfare Director W. S. Terry Jr., Baton Rouge, newspapers reported, July 3. C. Ellis Henican, chairman of the state welfare board, was elected chairman of the organization. The council will consist of representatives from area councils which will be set up throughout the state, representatives of all agencies operating in the fields of health, welfare and recreation. It will act only in an advisory capacity to the local groups operating their own programs. An area council is already functioning in New Orleans, it was said.

MAINE

Dr. Bittner Receives Alvarenga Prize.—The College of Physicians of Philadelphia awarded the Alvarenga Prize on July 14 to John J. Bittner, Ph.D., of the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, in recognition of his studies on cancer. Dr. Bittner received his degree of doctor of philosophy at the University of Michigan, Ann Arbor, in 1930. He was assistant in cancer research at Michigan from 1927 to 1930, when he went to the Jackson Memorial Laboratory as research associate. He has been a member of the board of

directors and assistant treasurer there since 1934 and acting treasurer since 1936. He has been special cancer investigator for the U. S. Public Health Service since 1932. Subjects covered by his research include the genetics of transplantable and spontaneous cancer in mice, hybridization and transplantable normal tissue.

MARYLAND

Typhoid Outbreak.—Twenty-three cases of typhoid were reported to the state department of health in an outbreak in the Mount Savage section of Western Baltimore, newspapers reported July 13. The source of the outbreak had not been determined at the time of this report. The first case was reported on June 20. A total of 1,117 persons had been given their first inoculation against the disease and 808 had received their second, the report stated.

MICHIGAN

New Director of Epidemiology.—Dr. Wallace M. Chapman, formerly director of district health unit number 3 at Charlevoix, has been appointed director of the bureau of epidemiology of the Michigan State Department of Health. Dr. James W. Chapman, director of the bureau of maternal and child health of the Missouri State Department of Health, has been named director of the health district, with offices in Charlevoix. The changes were effective on July 1, newspapers reported.

Pathologist Retires from Faculty.—Dr. James E. Davis, for many years professor of pathology at Wayne University College of Medicine, Detroit, has retired from that position. At the recent alumni reunion of the college, Dr. Davis was presented with a gift by Dr. Osborne A. Brines on behalf of the faculty. Dr. Davis graduated in 1896 at Wayne, then known as the Detroit College of Medicine and Surgery. In more recent years he also served for a time on the faculty of the University of Detroit dental department.

MISSOURI

Five Hundred More Beds at St. Louis City Hospital.—A new thirteen story general hospital building costing about $2,000,000 and containing five hundred beds was dedicated at the St. Louis City Hospital recently. The building includes an emergency suite, surgical pavilion, eye, ear, nose and throat, urologic, gynecologic, obstetric, pediatric, fracture and prison wards, delivery suites, occupational therapy department, physical therapy department and research laboratories. Some features of the building include overhead viewing of surgery, built-in biplane fluoroscope for foreign body localization in the chest and piped gases; for example therapeutic oxygen is piped to the wards. The building is part of a general rebuilding and modernization of the city hospital group, which was initiated with the opening of the Malcolm A. Bliss Psychiatric Institute in 1939. A new power house was the next unit completed, a rebuilt four story outpatient department was occupied in October 1940, and a new service building was opened two months later.

Suit Charging Infringement of Estrone Patent.—A civil action brought by the president and board of trustees of St. Louis University against Hospital Liquids, Inc., New York, charging infringement of letters patent 1,967,350 to Doisy et al. covering the manufacture and sale of estrone (theelin) and estrone (theelin) preparations, was concluded early in March. The plaintiffs and the defendant agreed to a consent judgment involving a cash settlement, the amount of which has not been made known. The consent judgment was entered by Judge John P. Barnes in the United States District Court for the Northern District of Illinois. The consent judgment ordered and adjudged that the plaintiffs are the exclusive owners of United States letters patent 1,967,350, together with the exclusive right to recover damages and/or profits for the infringement thereof. The consent judgment further adjudged that letters patent 1,967,350 is good and valid in law and that the defendant, Hospital Liquids, Inc., had infringed the patent by selling products covered by the claims of the same. The consent judgment further adjudged that the defendant be enjoined and restrained from making, selling or using any of the subject matter as defined by the claims of said letters patent. The action is the first thus far brought on behalf of St. Louis University for infringement of letters patent 1,967,350, which covers the manufacture of the isolated crystalline hormone (pure crystalline estrone [theelin]).

MONTANA

Personal.—Dr. Thomas W. Collinson has been appointed health officer of Scobey.——Ludvig Gustav Browman, Ph.D., assistant professor of zoology and physiology at Montana State University, Missoula, has received a second grant in aid of $500 from the National Research Council for the continuation of his research on the effect of light on the growth and activity of rats, according to *Science*.

NEW YORK

Hospital Lacks Residents.—The Rochester General Hospital, Rochester, reported in its *News Letter* recently that the national emergency has made vacancies in its residencies in medicine, orthopedics, obstetrics and ophthalmology. Of eight new interns who reported for duty on July 1, four hold commissions in the Medical Reserve Corps and presumably will be allowed to complete only one year of the two year appointment, it was said.

New Hospital Building.—Ground was broken for a new building for St. Mary's Hospital, Rochester, at a recent ceremony. The new home of the 84 year old hospital will have a capacity of three hundred and seventy-five beds and will cost about $1,000,000. It will be in a novel design described as an "end to end Y," with six floors. The present building will be used for the outpatient department, for educational purposes and as a meeting place for groups affiliated with the hospital.

Annual Chautauqua Meeting.—The annual Interstate Medical Meeting sponsored by the Medical Society of Chautauqua County was held in Chautauqua, July 30. The morning program began with a round table discussion of "Treatment of the Menopause," by Drs. Louis A. Siegel, Francis D. Leopold and Gilbert M. Beck, Buffalo, as participants. Drs. Arthur C. Ernstene and George Crile Jr., Cleveland, made addresses on medical and surgical aspects, respectively, of "The Present Status of Chemotherapy," with Dr. George W. Cottis, Jamestown, president-elect of the Medical Society of the State of New York, opening the discussion, and Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, gave an address entitled "American Medicine Prepares." In the afternoon Dr. Fishbein spoke at a public meeting on "Medicine Moves Forward." At a luncheon at the Hotel Athenaeum Dr. William D. Johnson, Batavia, was the speaker.

New York City

Three New Appointments at Cornell.—Appointments to three professorships have been announced by Cornell University Medical College. Dr. William Dock, professor of pathology at Stanford University School of Medicine, and pathologist to the Stanford University Hospitals in San Francisco, has been appointed professor of pathology at Cornell and pathologist to New York Hospital. Dr. Dock graduated from Rush Medical College, Chicago, in 1923 and joined the Stanford faculty in 1926 as an instructor. He became professor in 1936. Dr. David P. Barr, Busch professor of medicine at Washington University School of Medicine and physician in chief of Barnes Hospital, St. Louis, has been appointed professor of medicine and physician in chief to New York Hospital. Dr. Barr graduated from Cornell in 1914 and was on the faculty from 1916 to 1924, when he went to Washington University. He now succeeds Dr. Eugene F. Du Bois, who has been made professor of physiology and head of the department of physiology and biophysics. Dr. Du Bois has been associated with Cornell since 1912 except for the war years 1917-1919, when he served in the U. S. Navy. He has been professor of medicine since 1930.

NORTH DAKOTA

Outbreak of Encephalitis.—Twenty-five cases of encephalitis in the period July 1-12 and 35 since the beginning of the year were recently reported to the U. S. Public Health Service by Dr. Maysil M. Williams, state health officer. Seventeen of the cases occurred in Cass County, the first having been reported on July 1. The first 4 of these cases were diagnosed as encephalomyelitis, and a definite history of equine encephalomyelitis was found on the farm where 1 patient lived. Twenty-four of the 35 cases were in adults and 11 in children under 15. Four were in infants 1 year old or younger. For the first six months of 1941 280 cases have been reported for the entire country. For the calendar year 1940 there were 1,217 for the country as a whole.

OREGON

University News.—Dr. Anton J. Carlson, Chicago, delivered the annual commencement address at the University of Oregon Medical School, Portland, June 6, on "A New Frontier in Medicine: The Problem of Subclinical Diseases."

Postgraduate Lectures.—A course of lectures on obstetrics and pediatric surgery was presented during June in ten towns under the auspices of the Oregon State Medical Society in cooperation with the division of maternal and child health of the Oregon State Board of Health. The lecturers were Drs. William J. Dieckmann, associate professor of obstetrics and gynecology, University of Chicago, The School of Medicine, and Herbert E. Coe, Seattle. The towns were La Grande, The Dalles, Bend, Klamath Falls, Medford, Marshfield, Eugene, Salem, Astoria and Portland. This is the second course of its type; the previous one was presented in May 1939.

SOUTH DAKOTA

State Medical Election.—Dr. Nelius J. Nessa, Sioux Falls, was chosen president-elect of the South Dakota State Medical Association at the annual meeting at Mitchell in May, and Dr. Bertrand M. Hart, Oneida, became president. Dr. Joseph C. Ohlmacher, Vermillion, was elected vice president and Dr. Clarence E. Sherwood, Madison, secretary. Next year's meeting will be in Sioux Falls.

TENNESSEE

Joint Health Unit.—A joint health unit for Chattanooga and Hamilton County was placed in operation, July 1, with Dr. Fray O. Pearson, county health director, as director and Dr. William C. Sanford, city health commissioner, as assistant director.

Society News.—Dr. Charles R. Thomas, Chattanooga, addressed the Hamilton County Medical Society in Chattanooga, July 3, on "Pulmonary Embolism in Heart Disease." Dr. Robert C. Robertson spoke, August 7, on "Principles of Fracture Treatment."——Drs. John J. McCaughan and Giles A. Coors, Memphis, addressed the Shelby County Medical Society, July 1, on "Sarcoma of the Vulva" and "Calcification of Ovaries" respectively.

VIRGINIA

New Health Officers.—Dr. Aaron Wilson Brown, formerly of Rochester, Pa., has been appointed venereal disease control officer of Richmond. He succeeds Dr. Clyde F. Ross, who served on a part time basis.——Dr. Arthur H. Cummings, formerly of Binghamton, N. Y., has been appointed health officer of Portsmouth.——Dr. Louise Fry Galvin, Richmond, has been appointed to the newly created position of pediatric consultant of the orthopedic division of the crippled children's bureau in the state department of health.

WASHINGTON

Society News.—Speakers at the final meeting of the season of the King County Medical Society, Seattle, June 2, were Drs. Loren G. Shroat on "Injection Treatment of Hernia"; Souren H. Tashian, "Injection Treatment of Hemorrhoids," and Edwin A. Nixon, "Injection Treatment of Varicose Veins."

WISCONSIN

Teacher of Pharmacy Dies.—Edward Kremers, Ph.D., director emeritus of the school of pharmacy of the University of Wisconsin, Madison, died, July 9, aged 76. Dr. Kremers graduated in pharmacy at Wisconsin in 1886 and took a B.S. degree in 1888 and Ph.D. in 1890 at the University of Goettingen, Germany. He became instructor in pharmacy at Wisconsin in 1890 and two years later became professor of pharmaceutic chemistry and director of the course in pharmacy. In 1913 he started the first pharmaceutic experiment station in the United States and remained its head until his retirement in 1935. Since retiring he had been a member of the state board of pharmacy. Dr. Kremers was chairman of the committee on volatile oils and related subjects of the U. S. Pharmacopeia Revision Committee in 1900-1910. He was co-editor of the Standard National Dispensatory. Many honors had come to Dr. Kremers, including the Remington Medal in 1930, honorary degrees from the University of Michigan and the Philadelphia College of Pharmacy and Science, and honorary membership in French and German societies of pharmacy. He was honorary president of the recently established American Institute of the History of Pharmacy. In 1940 he received a bronze plaque of himself at a testimonial dinner held in Madison by three hundred Wisconsin pharmacists.

WYOMING

Rocky Mountain Medical Conference.—The third biennial Rocky Mountain Medical Conference will be held at the Canyon Hotel, Yellowstone National Park, September 2-4. Included among the speakers will be:

Dr. Frank H. Lahey, Boston, President of the American Medical Association, Medical Problems of Today; Management of Lesions of the Stomach, Duodenum and Jejunum.
Dr. John R. Nilsson, Omaha, The Transportation and Treatment of Severe Fractures by the Open Method.
Dr. Arnold S. Jackson, Madison, Wis., Reducing the Mortality of Perforated Appendicitis; Acute Surgical Conditions of the Abdomen.
Dr. Winchell McK. Craig, Rochester, Minn., Role of the Protruded Intervertebral Disk in the Production of Low Back and Sciatic Pain; Reaction of the Central Nervous System to Trauma: Diagnosis and Treatment.
Dr. Norman F. Miller, Ann Arbor, Mich., The Human Cervix in Health and Disease; The Bloody Complications of Obstetrics.
Dr. Guy A. Caldwell, New Orleans, Sulfanilamide in Compound Fractures; Treatment of Fractures of the Upper Extremity of the Humerus.
Dr. Rosco G. Leland, Chicago, Director, Bureau of Medical Economics, American Medical Association, Medicine Prepares; Current Social Experiments in Medicine.
Dr. Alexis F. Hartmann, St. Louis, Management of Severe Diarrheal Acidosis and the Alkalosis of Vomiting; Treatment of Upper Respiratory Tract Infections.
Dr. Clarence M. Hyland, Los Angeles, Convalescent Human Serum Therapy; Serum and Plasma as Blood Substitutes.
Dr. James G. Carr, Chicago, Clinical Diagnosis of Coronary Occlusion; Cardiac Irregularities and Paroxysmal Tachycardia.
Dr. J. Peerman Nesselrod, Evanston, Ill., Anal Infections; Proctoscopic Cinematography.

The medical societies of Colorado, Montana, New Mexico, Utah and Wyoming form the Rocky Mountain Medical Conference. This year the Wyoming State Medical Society will be host to the conference.

MIDWAY ISLANDS

Midway Islands Physicians Organize Society.—Physicians and dentists stationed with the Third Defense Battalion, Fleet Marine Force, and others with civilian contractors in defense construction on the Midway Islands in the North Pacific Ocean have organized the Midway Islands Medico-Dental Society with Dr. Khatchig H. Terts as president and Lieut. (j. g.) William R. Franklin, D. C., U. S. Navy, as secretary. The society plans to hold monthly meetings when ships calling at the islands bring visiting physicians and dentists. The first meeting was held on June 12 with the following program:

Lieut. Comdr. Julian Love, M.C., U. S. Navy, Early Diagnosis of Thromboangiitis Obliterans; also Tetanus Toxoid.
Lieut. Franklin and Lieut. (j. g.) Ralph W. Geise, M.C., U. S. Navy, Ludwig's Angina (case report).
Lieut. Comdr. Roy F. Cantrell, M.C., U. S. Navy, Thrombophlebitis; also Meningococcic Meningitis.

PHILIPPINE ISLANDS

Association Approves School Administration.—The Philippine Medical Association at its recent annual meeting adopted a resolution commending Dr. Antonio Sison, dean of the College of Medicine, University of the Philippines, on his administration of the college. An editorial in *The Journal of the Philippine Medical Association* points out that in the four years since Dr. Sison was appointed dean the faculty has been strengthened, limitation and rigid selection of students have been enforced, research and scholarship on the part of the faculty have been encouraged, the curriculum has been simplified, methods of teaching have been modernized and conferences have been instituted for improvement in the work of students and faculty.

GENERAL

Society News.—The twenty-sixth National Recreation Congress will be held in Baltimore, September 29-October 3, at the Lord Baltimore Hotel. This year's program will include discussion of recreation for men in military service and recreation as a factor in civilian defense.——The Polish Medical and Dental Association of America will meet in Grand Rapids, Mich., August 21-23, in a combined meeting with the Polish-American National Bar Association and the National Federation of Polish Art Clubs.——The annual meeting of the International Association of Milk Sanitarians will be held in Tulsa, Okla., October 27-29. The president is Mr. Leslie C. Frank, U. S. Public Health Service, Washington, D. C., and Mr. C. Sidney Leete, New York State Department of Health, Albany, is secretary.

Air Hygiene Foundation Changes Name.—The Air Hygiene Foundation of America, Inc., has changed its name to the Industrial Hygiene Foundation of America, Inc., to

describe more clearly the expanding activities and services of the organization, it is announced. When the foundation was organized in 1935 its main emphasis was on silicosis. With the rapid advances in industrial hygiene and with new occupational health problems, the work has steadily broadened. A study is now under way in collaboration with the U. S. Public Health Service to help reduce sick absenteeism in heavy industries. Other studies include roentgen ray technics for large scale physical examinations in industry, control of toxic fumes and gases, exhaust ventilation for health protection of employees and investigations of "protector" dusts to combat dust diseases.

Prevalence of Poliomyelitis.—The U. S. Public Health Service reported on July 18 that 187 cases of poliomyelitis had been reported for the week ended July 12, as compared with 82 cases for the preceding week. The highest incidence was in the South Atlantic and East South Central states, which reported 127 cases. In the first twenty-eight weeks of this year a total of 983 cases had been reported in the country as a whole, as compared with 948 for the same period in 1940.—— Newspaper reports indicate that 69 cases have been reported for the year up to August 2 in Illinois. The number of cases current in Tennessee on August 2 was said to be 53. These are centered in Coffee, Franklin, Bedford and Davidson counties. New York City has had only 17 cases from January 1 up to July 30; the first death occurred during the week ended July 30, according to the New York *Times*. Reports dated July 16 gave 70 cases as the total for Alabama since June 1 and 131 for Georgia between June 1 and July 15.

Provisional Mortality Figures for 1940.—The steady decline in the mortality rate in recent years appears to have been checked in 1940, the Bureau of the Census reports in its announcement of crude death rates based on provisional mortality statistics for 1940. According to these tabulations there were 1,417,257 deaths in 1940, an increase of 29,460. The rate was 10.8 per thousand, compared with 10.6, the final rate for 1939. The rate appears to have been higher in thirty states and the District of Columbia, lower in thirteen states and the same in five states. The largest increase was reported for Nevada and the largest decrease for New Mexico. The highest rates were: District of Columbia 13, Vermont 12.8, New Hampshire 12.7, Nevada 12.7, Maine 12.5, Delaware 12.2, Maryland 12.1 and Florida 12.1. The lowest rates were: North Dakota 8.2, South Dakota 8.5, Wyoming 8.5, Oklahoma 8.8, Arkansas 8.8 and Utah 8.9 per thousand of enumerated population. Cities with the highest rates were: Sacramento, Calif., 16.5; New Orleans 16.4; Nashville, Tenn., 16.2; Tacoma, Wash., 16, and Albany, N. Y., 15.

Grants for Infantile Paralysis Research.—The National Foundation for Infantile Paralysis announced new grants totaling $195,030, July 25. Among the larger grants are the following:

University of Michigan School of Public Health, Ann Arbor, $40,000 to provide facilities for the study of virus diseases.

National Organization for Public Health Nursing, New York, two grants totaling $23,400 to encourage nurses to study orthopedic public health nursing, to aid in developing centers for such study and to prepare a manual on orthopedic care.

Children's Hospital, Boston, $6,300 to finance continued study of effects of infantile paralysis on the growth of the lower extremities and a new study of the effect of prolonged bed rest on development of calculi in the urinary tract of patients.

Strong Memorial Hospital, Rochester, N. Y., $9,200 to continue studies to determine functional indexes in normal and abnormal locomotion.

Michael Reese Hospital, Chicago, $7,930 to permit continuation of previous studies in various aspects of the treatment of infantile paralysis and some aspects of the after-effects of the disease.

Johns Hopkins University School of Medicine, Baltimore, $9,300 for studies of antibodies neutralizing the infantile paralysis virus.

City Hospital, Cleveland, $5,300 for a study of infantile paralysis in experimental animals.

New York State Health Department, Albany, $12,000 to study the prevalence of apparently healthy carriers.

Physical Therapy Meetings.—The American Congress of Physical Therapy and the American Occupational Therapy Association will hold their annual meetings at the Hotel Mayflower, Washington, D. C., September 1-5. Among speakers at the physical therapy meeting will be:

Dr. Walter S. McClellan, Saratoga Springs, N. Y., The Role of Spas in Medical Preparedness.

Howard A. Carter, B.S. in M.E., secretary, Council on Physical Therapy, American Medical Association, Chicago, Threshold of Electrical Stimulation.

William F. Wells, B.S., Philadelphia, Radiant Disinfection of Air.

Dr. Fred B. Moor, Los Angeles, Hydrotherapy in Local Injuries and Infections.

Dr. Lewis Clark Wagner, New York, Evaluation of Operative Procedures in Spastic Paralysis.

Dr. Edmund Jacobson, Chicago, Cultivated Relaxation for the Elimination of Nervous Breakdowns.

Dr. Henry L. Williams, Rochester, Minn., Physical Treatment of Indurative Headache.

There will be one joint session of the two organizations with the following speakers, among others:

Dr. Winthrop M. Phelps, Baltimore, Correlation of Physical Therapy and Occupational Therapy in the Treatment of Cerebral Palsy.

Dr. Robert Lee Patterson Jr., New York, Obstetric Paralysis.

Dr. Alfred R. Shands Jr., Wilmington, Del., Operative Treatment of the Lower Extremity in Infantile Paralysis.

Dr. Robert L. Bennett Jr., Warm Springs, Ga., Adequate Home Treatment for the Patient with Poliomyelitis.

The occupational therapy program announces sessions devoted to children with heart disease, neuropsychiatric aspects of occupational therapy, tuberculosis, methods used in the facilities of the Veterans Administration and national defense. Dr. Nathan H. Polmer, New Orleans, is president of the American Congress of Physical Therapy and Mr. Everett S. Elwood, Philadelphia, of the American Occupational Therapy Association.

FOREIGN

British Students to North American Schools.—Twenty-six British medical students have been chosen to study in nineteen medical schools of the United States and Canada under the auspices of the Rockefeller Foundation, the *British Medical Journal* reports. Candidates were chosen by the deans of medical schools. Nearly a hundred applications were received and nearly two thirds of the number were interviewed by the committee of selection, headed by Sir John Stopford, Manchester.

Government Services

Dr. DeLien in New Assignment

Dr. Horace DeLien, special physician in tuberculosis control of the Indian Service for California, Nevada and Utah, with headquarters in San Francisco, has been made special expert in tuberculosis to succeed Dr. Joseph D. Aronson, who has been called to army duty. Dr. DeLien will continue studies in vaccination with BCG which were initiated by Dr. Aronson in North Dakota, South Dakota, Wyoming, Arizona and Alaska. In addition he will continue to supervise the control program in the states under his former assignment.

New Public Health Workers Assigned

The U. S Public Health Service announces that forty-one physicians, thirty-nine nurses, fifty-one sanitary engineers and three laboratory technicians have recently been assigned to state and local health departments in defense areas to help in public health problems created by the emergency. These workers first spent a month at the National Institute of Health in Bethesda, Md., for orientation courses. Funds have been provided for the training of engineers for malaria control work. This training will be given at a field station in Norfolk, Va., in cooperation with the Virginia State Health Department.

Government Seeks Medical Personnel

The U. S. Civil Service Commission announces examinations for three types of medical positions. Junior medical officer positions at St. Elizabeths Hospital in Washington, D. C., at $2,000 a year are to be filled, including rotating internships and psychiatric residencies. To qualify for the rotating internships, applicants must be fourth year students in recognized medical schools and must show completion of the course before June 30, 1942. Graduates in medicine who have already served a rotating internship are offered a postgraduate internship of one year of psychiatry. Applications will be accepted until November 15.

Medical technical assistant positions at $2,000 a year and medical guard attendant positions at $1,620 a year will be filled in the mental hygiene division of the U. S. Public Health Service. Applicants must be registered nurses or have been honorably discharged (within ten years preceding the examination) from the Medical Corps of the army or navy or must have had three years' service as guard attendant in a federal penal or correctional institution. Applicants for the positions of technical assistant must have had responsible training or experience in clinical laboratory technic, pharmacy or roentgen ray laboratory technic. Applications for these positions will be accepted until further notice. Information and application forms may be obtained at any first or second class post office or from the Civil Service Commission in Washington, D. C.

Foreign Letters

LONDON

(From Our Regular Correspondent)

June 21, 1941.

Health in War Time

In a previous letter (THE JOURNAL, Dec. 7, 1940, p. 2014) the minister of health, Mr. MacDonald, was quoted to the effect that the national health had actually improved under war conditions. The health statistics for 1939, in which there were eight months of uneasy peace and four months of war, were almost uniformly better than those of 1938, which in turn were an advance. Nearly a year and a half of war, on a scale which demands the greatest possible amount of the national energies, has elapsed since the period covered by Mr. MacDonald's survey, and a similar report can be made. All the sources of information available show that the nation has stood up remarkably well to war conditions. In the last few months of 1940 and the spring of 1941 there was an epidemic of influenza, which was attributed to an undetermined type of virus. But there were no serious cases. There was also early in 1940 an epidemic of rubella. This was relatively harmless. Otherwise, in spite of crowded air raid shelters and the domestic disorganization due to evacuation of children and others to safer areas, we have remained free from any major epidemic. In spite of prolonged hours of work and the withdrawal of most of the younger men for military service, industrial sick records do not show any great increase of illness.

So much for physical illness. It might be expected that the strain of this world war, with the new horror of the bombing of crowded cities, in which eighty thousand persons—almost all unarmed men, women and children—have been massacred or mutilated, would have had some mental effect on the population at large. But it preserves its characteristic calm and balance. There are of course some sufferers from shock among those exposed to the deafening explosion of bombs, of whom some have narrowly escaped death. But it has been found that the majority of these were already of the type liable to break down in any unexpected or severe emergency. The air raids have revealed rather than created them. No effect has been observed on the definitely insane or epileptic.

In spite of the dietetic restrictions, which limit the consumption of such important foods as meat (24 cents worth weekly), butter (4 ounces weekly), sugar (8 ounces weekly) and cheese (1 ounce weekly), the nutrition of the people remains excellent for the reason that so many other foods are not rationed. Indeed, Lord Horder has pointed out that for many elderly and sedentary persons the restrictions have probably been beneficial.

The position as regards tuberculosis—a disease very dependent on nutrition—is satisfactory. During the last fifty years there has been a continuous decline of this disease and at an accelerating rate. Thus the death rate from all forms in 1927 was 972 per million persons living; in 1937 it was 695. But during the last great war and for two years afterward the incidence increased. Since then there has been a steady and continuous improvement. Up to the present there has been no notable increase ascribable to the present war.

War Time Nurseries

The war has disturbed family life by evacuation from areas liable to bombing and by the increased employment of women in industry. The need has therefore arisen of making some form of nursery provision for young children. The government is now providing war time nurseries both for evacuated children and for women in employment. They are administered by a joint staff of the Ministry of Health and the Board of Education, but the local authority is made responsible for their provision and the special war time arrangements. There are two types of nursery. The first type is the part time nursery, which provides for children between the ages of 2 and 5 years, is open approximately for school hours and is under the direction of a teacher. Such nurseries are suitable for children evacuated with or without their mothers and also for children whose mothers are either in part time employment or are able to make other arrangements for the care of their children before the nursery is opened in the morning and after it is closed in the evening.

The second type is the whole time nursery. This provides for the full day time care and maintenance of children up to the age of 5 years. It is required when women are in full time employment and cannot arrange for the care of their children at any time during the day. They are open for periods up to fifteen hours a day and provide meals and facilities for resting and bathing. A trained nursing staff is essential. The local education authority arranges for the social training and occupation of children between the ages of 2 and 5 years. At whole time nurseries, where children are cared for all day and receive all their meals, mothers pay 24 cents daily; at part time nurseries, where no meals are provided, 6 cents daily. But no payment is required from evacuated mothers who are not in employment. The American Red Cross has made a gift for the conditioning of huts and premises to serve as nurseries for evacuated children.

Soldiers Should Be Taught First Aid

A "Lance-Corporal" has made in the *Lancet* a suggestion so sensible that, following the shavian paradox, one could say "This is so obvious that it has been overlooked." The lance-corporal points out that the soldier is taught how to kill and destroy, how to operate his weapons and how to protect himself against similar weapons, but he does not receive lessons in how to save a comrade's life. The army books say that in the rear of our front we shall have regimental aid posts and behind them a temporary hospital. Therefore it is argued that all wounded shall receive prompt treatment. But recent experience in France showed that there is no such thing as a "front." Mechanized forces move too quickly for that, so that small bodies of men are isolated from the main body. It follows that every soldier should know how to set broken limbs, stop arterial bleeding and have a sound knowledge of first aid. When the lance-corporal mentioned the matter to his medical officer he was told "Bad first aid is often worse than no first aid." To this his answer is "Every soldier must know how to apply good first aid." Though medical officers are busy men, they would be only too pleased to give lectures.

The Protection of Patients Against Attacks of Poison Gas

The Ministry of Health is sending warnings to the public to be prepared for gas attacks. They should see that their respirators are kept in good order and always have them at hand. In hospitals special questions arise. For patients suffering from certain disabilities such as chronic asthma, heart disease or facial distortions, special respirators with outlet valves or helmet respirators are issued. It is suggested that the respirators be kept by the patients' beds where they will be ready for instant use. Soon after admission each patient who is in a suitable condition should try on his respirator to see that it fits properly. It may be possible to institute a weekly gas practice for the staff and for patients who are in a suitable condition.

Medical supplies, like food, should be protected against contamination with gas. The normal conditions of storage of medical and surgical supplies in warmed and ventilated build-

ings should provide all that is practicable of protection against liquid contamination. Some additional protection can be afforded by using existing stocks of waterproof sheeting, batiste, cellophane or other impermeable material as a covering for unprotected stores or for stores whose nature or wrapping do not themselves provide protection. Surgical dressings, cotton wool or bandages wrapped in paper, cardboard or cartons would not be contaminated by exposure to vapor, provided the wrappings are undamaged. Traces of vapor could be removed by opening them out and airing them for an hour or so in a clean, well ventilated atmosphere. If contaminated by liquid, it is doubtful whether any decontamination treatment would be satisfactory, and destruction by burning may be unavoidable. Gum elastic catheters, surgeons' gloves and fine rubber drain sheeting are unlikely to stand boiling and, if contaminated by liquid, should be destroyed. Metal instruments can be decontaminated by immersion for thirty minutes in boiling water or swabbing with a solvent.

NEWS FROM GERMANY

(Compiled from Recent German Periodicals)

Required Reports on Hospitalized Soldiers

Irregularities in notifying military authorities of the hospitalization, discharge or death of soldiers treated in public or private institutions and in failing to furnish the case histories and other necessary information regarding the legal status of such men has caused confusion in the military records and anxiety among relatives. It has happened that hospitalized men were recorded as absent without leave or classified among the missing. In order to forestall further irregularities, a number of regulations have been announced. Hereafter, civil hospitals are required promptly to report to the central military bureau in Berlin responsible for the nation's casualty records the admission, discharge or death of all hospitalized soldiers. Full case histories must be kept, including notations relative to the subsequent needs for care and possible claims on the part of the hospitalized men. When men are transferred to other hospitals, copies or summaries of their case histories must be sent along, together with roentgen film reproductions, if these are necessary or requested. On discharge for further military or naval service or in the event of death, copies of case histories and roentgenograms should be transmitted, on request, to the military or naval authority involved. Case histories originating during army or navy medical care should be returned in their original form. Original records may be temporarily released by public or private hospitals for photostatic purposes.

Louvain University Destroyed Again

The library of the University of Louvain has suffered what seems to amount to approximate annihilation. Damaged in the World War and rebuilt largely with the financial aid of American well wishers, it was again destroyed in May 1940. Of the 900,000 volumes only 15,000 survive, and of 800 manuscripts only 15. Three thousand collections of periodicals were completely destroyed by fire; likewise, 811 incunabula and 200 valuable engravings, including some by Dürer and Holbein, and the 22,606 photographs of all known Coptic manuscripts. (From the *Deutsche medizinische Wochenschrift* **67**:577 [May 23] 1941.)

Venereal Disease Census

In June 1940 a census was taken throughout Germany of all venereally infected persons treated by a physician for the first time. One hundred and twenty-two thousand men and 75,000 women were so reported. This seems to indicate that the morbidity rate for venereal diseases during the present war did not increase, contrary to usual war time expectations. However, an increase in female cases of gonorrhea was reported. The increase is attributed to the use of more thorough methods of examination.

Enforced Change of Name of Evangelical Hospitals

The names of the following evangelical hospitals have been changed: Bethanien is now the Sophienkrankenhaus; Bethesda was changed to Elise Averdieck; Bethlehem to Anschar; Ebenezer to Albrechtkrankenhaus; Elim to Krankenhaus Hohe Weide; Jerusalem to Krankenhaus am Moorkamp; Tabea to Krankenhaus am Falkenstein (Blankenese), and Siloah becomes Albertinenkrankenhaus. In the Siloah hospitals for men and young women the name Siloah has likewise been replaced by Albertinen.

New Medical Periodical

The first issue of a new periodical, called *Vitamine und Hormone*, central organ of vitamin and endocrine research, was published in the spring of 1940. The periodical will present original articles and related scientific material. Publication will perhaps be on a monthly basis. The periodical is edited by Prof. B. C. P. Jansen of Amsterdam, Prof. A. Scheunert of Leipzig, Prof. H. Siebke of Bonn and Prof. W. Stepp of Munich.

Medical Care for the Underprivileged

Since the end of March of this year, social welfare clients in Vienna will no longer have to accept medical treatment from physicians of the poor (armenärzte) but are free to consult sick fund physicians (kassenärzte). A certificate good for the year is furnished them by the local welfare stations.

Marriages

JEAN MCNUTT MARTIN, Middlebrook, Va., to Mr. Ralph Allen Glasgow of Roanoke in Brownsburg recently.

WILLIAM F. HUGHES JR., Indianapolis, to Miss Wanema Alter Dickey of Carlisle, Pa., in Baltimore, June 28.

RUSSELL W. BLANCHARD, Council Bluffs, Iowa, to Miss Muriel W. Alexander of Oglesby, Ill., in June.

WILLIAM SOUTHARD SCOTT, Spartanburg, S. C., to Miss Lucille Loggins of Dickson, Tenn., June 11.

JOHN ROBERT HILSENBECK, Jenkins, Ky., to Miss Florence Burns of Milligan College, Tenn., June 19.

WILLIAM KEEFER BRUMBACH, Belleville, N. J., to Miss Mattie Evelyn Boone of Edgefield, S. C., in June.

JAMES BARRETT THOMPSON, Rochester, N. Y., to Miss Elizabeth Allen in Ann Arbor, Mich., June 14.

JAMES BYRON CARTY, Burlington, N. J., to Miss Allie Brown Rendleman at Salisbury, N. C., June 14.

BENJAMIN HACKETT HARDING, Yadkinville, N. C., to Miss Eula Blanche Bare of Jefferson in June.

EDWARD VERNON POLLARD, Parsons, Tenn., to Miss Dorothy Templeton at Gulfport, Miss., June 7.

ISAAC C. KNOX JR., Vicksburg, Miss., to Miss Emmette Brown of Birmingham, Ala., in June.

ROBERT O. NORTHWAY to Miss Georgia Fay Kasischke, both of Mount Pleasant, Mich., June 21.

MYRON GORDON HOWLE, Summerton, S. C., to Miss Carolyn Giles Ariail of Greenville, June 12.

GEORGE K. HAMMERSLEY, Indianapolis, to Miss Mary Ellen Lemen of Osgood, Ind., May 16.

RICHARD DENMAN CROW, Shreveport, La., to Miss Mary Jane Eager of Jackson, Miss., June 5.

DENNIS S. MEGENHARDT, Indianapolis, to Miss Mary Virginia Kendall of Marion, Ind., May 25.

CORNELIUS A. SAFFERT, New Ulm, Minn., to Miss Helen M. Kienlen of St. George, May 26.

WINTER C. WALLACE to Miss Mildred Taylor, both of Ruthfordton, N. C., in June.

JOHN H. MOWRY to Miss Virginia A. Davenny, both of Conneaut, Ohio, June 14.

RALPH G. NICHOLS to Miss Virginia Bruce, both of Knoxville, Tenn., June 21.

DUNCAN D. MONROE, Alton, Ill., to Miss Alberta Martin of Godfrey, June 1.

HARRY E. MURPHY to Miss Helen Catt, both of Franklin, Ind., June 1.

Deaths

William Herman Myers ✠ Savannah, Ga.; University of Tennessee Medical Department, Nashville, 1901; member of the House of Delegates of the American Medical Association from 1929 to 1941; past president of the Medical Association of Georgia; fellow of the American College of Surgeons; at one time a first lieutenant in the medical reserve corps of the United States Army; served during the World War; on the staffs of the Telfair Hospital and St. Joseph's Hospital; aged 62; died, July 17, in Highland, N. C., of coronary thrombosis.

George Elihu Bellows, Laguna Beach, Calif.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1885; member of the Missouri State Medical Association and the American Academy of Ophthalmology and Otolaryngology; for many years chairman of the public health and welfare committee of the chamber of commerce of Kansas City, Mo.; at one time on the staffs of St. Luke's, St. Margaret's and the Research hospitals, Kansas City, Mo.; aged 79; died, June 19, of heart disease.

Allen J. Black ✠ Major, United States Army, retired, Richmond, Va.; Medical College of Virginia, Richmond, 1884; veteran of the Spanish-American and World wars; entered the medical corps of the United States Army July 1, 1920 as a major and retired Jan. 27, 1928 for disability in line of duty; past president of the Roanoke Academy of Medicine; aged 76; died, June 25, of myocarditis and arteriosclerosis.

Robert Boyd Bogle, Nashville, Tenn.; University of Nashville Medical Department and Vanderbilt University School of Medicine, Nashville, 1894; also a dentist; past president of the American Dental Association; professor emeritus of clinical dental surgery at Vanderbilt University School of Medicine; dean of the Vanderbilt University School of Dentistry from 1919 to 1926; aged 66; died, May 25.

Burton Haseltine ✠ Chicago; Hahnemann Medical College and Hospital, Chicago, 1896; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staff of the Henrotin Hospital; consulting otologic surgeon, Cook County Hospital and the Illinois Masonic Hospital; aged 66; died, July 12, of heart disease.

William George Bouse, Goff, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1906; member of the Kansas Medical Society; served during the World War; past president of the Nemaha County Medical Society; aged 65; was killed in June when the automobile in which he was driving was struck by a train.

Joseph T. Abshire ✠ Kaplan, La.; College of Physicians and Surgeons, Baltimore, 1889; past president of the Vermilion Parish Medical Society; formerly member of the school board of Leroy and postmaster; for many years parish coroner and mayor of Kaplan; aged 72; died, June 22, of heart disease, arteriosclerosis and hypostatic pneumonia.

Charles Daniel Johnson ✠ Tulsa, Okla.; St. Louis University School of Medicine, 1914; at one time head of the department of physics and chemistry at the Northwestern State Normal School, Alva; assistant in chemistry, 1914-1915, assistant in pathology, 1915-1916 and instructor in pathology, 1916-1917 at his alma mater; aged 59; died, June 24.

William Harrison Slaughter, Darien, Conn.; Columbia University College of Physicians and Surgeons, New York, 1907; health officer; on the associate staff of the Stamford (Conn.) Hospital and on the courtesy staff of the Norwalk (Conn.) Hospital; aged 62; died, June 4, of coronary thrombosis.

Carl Aticus Harris, Bessemer, Ala.; University of Alabama School of Medicine, Mobile, 1910; member of the Medical Association of the State of Alabama; fellow of the American College of Surgeons; served during the World War; on the staff of the Bessemer General Hospital; aged 54; died, June 22.

Nathaniel F. Cheever, Greenfield, N. H.; University of Vermont College of Medicine, Burlington, 1883; member of the New Hampshire Medical Society; past president of the Hillsboro County Medical Society; formerly member of the school board; aged 84; died, June 15, in Milford of arteriosclerosis

Frederick M. Brooks, Fairfax Station, Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1883; member of the Medical Society of Virginia; for many years bank president and member of the county school board; aged 82; died, June 21, of chronic myocarditis.

Martin Luther Hindley, Monroeville, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; member of the Ohio State Medical Association; formerly a member of the board of education; aged 71; was found dead, June 25, of heart disease.

Everett Chaney Robbins, Chillicothe, Ohio; Ohio State University College of Medicine, Columbus, 1917; member of the Ohio State Medical Association; served during the World War; aged 48; died, June 4, in the Chillicothe Hospital of cerebral hemorrhage.

Waitman T. Willey Dye, Grantsville, W. Va.; Starling Medical College, Columbus, 1886; member of the West Virginia State Medical Association; aged 80; died, June 26, of rheumatic valvular heart disease and carcinoma of the stomach.

Howard Murray Ritter, Williamsport, Pa.; Jefferson Medical College of Philadelphia, 1895; member of the Medical Society of the State of Pennsylvania; fellow of the American College of Surgeons; aged 71; died, June 1, of heart disease.

Edward William Hanlon ✠ San Francisco; College of Physicians and Surgeons, medical department of Columbia College, New York, 1893; on the staffs of St. Marys and St. Francis hospitals; aged 69; died, June 3, of coronary occlusion.

Frank Hollis Burnett, Brockton, Mass.; Dartmouth Medical School, Hanover, N. H., 1890; member of the Massachusetts Medical Society; on the staff of the Brockton Hospital; aged 74; died, June 21, of coronary thrombosis.

Frank Houston Gardner, Flat Rock, Ala.; College of Physicians and Surgeons, Baltimore, 1891; also a minister; aged 74; died, June 6, in Calhoun, Ga., of uremia, following injuries received in an automobile accident.

Thomas Earl Goyer, Jackson, Tenn.; Memphis Hospital Medical College, 1912; member of the Tennessee State Medical Association; aged 53; died, June 16, in the Memorial Hospital of hemorrhage due to gastric ulcer.

William Edgar Braswell, Sandy Ridge, N. C.; University of Georgia Medical Department, Augusta, 1907; formerly county coroner; aged 61; died, June 16, in a hospital at Winston-Salem of cerebral hemorrhage.

Vincent Pangolli Bell ✠ Greenville, S. C.; Medical College of the State of South Carolina, Charleston, 1923; aged 53; died, June 12, in the Johns Hopkins Hospital, Baltimore, of cirrhosis of the liver.

James M. Sheppard, El Dorado, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1897; member of the Arkansas Medical Society; aged 77; died, June 9, of myocarditis and nephritis.

Frederick William Youmans, Lewisville, Ark.; Rush Medical College, Chicago, 1891; member of the Arkansas Medical Society; aged 75; died, April 3, in the Josephine Hospital, Hope, of thrombosis.

Otis Fillmore Miller, Danville, Ky.; Southwestern Homeopathic Medical College and Hospital, Louisville, 1902; served during the World War; aged 76; died, June 9.

Robert Goldberg ✠ New York; University and Bellevue Hospital Medical College, New York, 1914; aged 52; died, June 13, in the Park East Hospital of uremia.

Gustav Frederick Boehme Jr., Los Angeles; Cornell University Medical College, New York, 1910; aged 53; died, June 7, of an overdose of a drug, self administered.

Charles John Edgar, North Hatley, Que., Canada; McGill University Faculty of Medicine, Montreal, 1887; served during the World War; aged 78; died, June 18.

Frank Harris, Trenton, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; aged 64; died, June 24, in St. Francis Hospital.

Luis C. Boneta, Rio Piedras, P. R.; Baltimore Medical College, 1908; member of the Medical Association of Puerto Rico; aged 55; died in June.

Harry Amant, Springfield, Ill.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1910; aged 61; died, June 27, in St. John's Hospital.

William Clare Green, Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1905; aged 72; died, June 17.

Robert Bruce Burwell, Moose Jaw, Sask., Canada; University of Toronto Faculty of Medicine, 1905; aged 64; died, June 3.

Stanley Thomas Cavins, Stanford, Ill.; Baltimore Medical College, 1903; aged 67; died, June 21.

Bureau of Investigation

CEASE AND DESIST ORDERS

Abstracts of Certain Federal Trade Commission Releases

The work of the Federal Trade Commission, in helping to protect the public against misrepresentation or fraud in the medical as well as other fields, has been greatly extended by the provisions of the Wheeler-Lea Amendment to the Federal Trade Commission Act. The Food, Drug and Cosmetic Act of 1938 added to the Food and Drug Administration's control of the advertising claims and statements made on the labels of medicine or on the carton or in the accompanying leaflet, whereas what might be termed collateral advertising, that which appears in newspapers and magazines and over the air, comes more actively under the purview of the Federal Trade Commission by virtue of the Wheeler-Lea Amendment.

THE JOURNAL has at various times commented on the activities of the Federal Trade Commission in this connection, even before the Wheeler-Lea Amendent gave it its added rights. In some cases the Commission may accept from the person or concern involved a stipulation that the objectionable practices or claims cited will be discontinued. In other cases the Commission issues what is known as a Cease and Desist Order, in which the individual or company cited is ordered to cease and desist from practices which have been declared objectionable. Abstracts of some of the orders issued during 1940 follow:

Atlas Short Wave Diathermy.—This was promoted by a Jacob L. Goldman, Los Angeles, alias J. L. Coleman, who traded as Atlas Health Appliance Company. On Dec. 12, 1940 the Federal Trade Commission issued a cease and desist order against Goldman to discontinue certain advertising misrepresentations. Among these were that his device or any other of substantially similar construction, when used by the unskilled lay public, constitutes a scientific, safe, harmless or effective means or method for the treatment of sinusitis, neuralgia and numerous other ailments, or that the mechanism aids in killing bacteria. Goldman also was to cease disseminating advertisements which failed to reveal that the unsupervised use of the device by persons not skilled in the diagnosis, analysis and methods of treatment of disease may result in serious and irreparable injury to health.

Beautiderm Midget.—This device, recommended for use in the electrolytic removal of hair, is put out by Electrolysis Associates, Inc., New York, who represented that it could be used at home for removing superfluous hair safely, painlessly and permanently. According to the findings of the Federal Trade Commission the use of this device by unskilled persons under conditions prescribed in the advertisements or under customary and usual conditions might result in serious or irreparable injury to health, such as local infections, erysipelas, skin burns, scarring and permanent disfigurement, and, moreover, the treatment would not be painless in untrained hands. On Dec. 16, 1940 the Commission ordered the Electrolysis Associates, Inc., and Louis Zinberg, an officer of the corporation, to discontinue the representations to which the Commission had objected. All of this in spite of the fact that in November 1938 Louis Zinberg, trading as Beautiderm Company, New York, had signed a stipulation with the Commission that he would cease advertising that his Beautiderm Midget would permanently destroy or prevent the regrowth of superfluous hair and could be self applied with absolute safety, unless in making such representations he would explain to the user that proper skill and care are necessary in employing the device. He also had promised to discontinue representing that the Beautiderm Midget constitutes the "one method advised by physicians as absolutely safe" so as to imply that they constitute the only so-called safe method of removing superfluous hair, when such is not a fact.

Blue Jay Foot Products.—On Dec. 7, 1940 the Federal Trade Commission reported that it had ordered the Kendall Company of Boston, which has a manufacturing division in Chicago under the trade name Bauer and Black, to cease and desist from certain misrepresentations in the advertising of its "Blue Jay Corn Plaster," "Blue Jay Bunion and Callus Plasters" and "Blue Jay Liquid Corn Remover." Among them were that corns have roots, that the Blue Jay products will prevent the formation or recurrence of corns or calluses, or that they constitute a new treatment for corns, calluses or bunions, or will instantly stop the pain caused by corns or calluses. The Commission declared that these representations were untrue and that the products cannot always be relied on entirely to remove the conelike portions of corns which project into the dermis. Back in 1916 the late Dr. Harvey W. Wiley, former chief of the Food and Drugs Division at Washington, reported in his book "1001 Tests" that Blue Jay Corn Plaster contained salicylic acid, which, as he pointed out, "is practically always the active ingredient of corn salves."

Delv.—On Dec. 29, 1940 the Federal Trade Commission ordered Primrose House, Inc., New York, to discontinue certain misrepresentations in the sale of this product, such as that "Delv" acts on the skin as do the natural fluids of the skin or that it serves the same purpose as these fluids; that it will cause wrinkles, large or unsightly pores or other imperfections to disappear from the skin; that it will nourish or rejuvenate the skin or create a new skin texture, or will keep the face young and the complexion beautiful. Still earlier (May 1935) a subsidiary of the concern, Primrose House Sales Company, Inc., had signed a stipulation with the Federal Trade Commission in which it agreed to abandon the use of certain allegedly false representations in the sale of Delv. The Federal Trade Commission reported, however, that in spite of this some of the misrepresentations had continued, and hence the necessity for the cease and desist order.

Kuhn's Remedy.—This product of the Kuhn Remedy Company, Chicago, was earlier known as "Kuhn's Rheumatic Remedy" and "Kuhn's Rheumatic Fever Remedy." On Dec. 5, 1940 the Federal Trade Commission ordered this concern to cease and desist from making certain misrepresentations in its advertising. Among these were that the product is a cure or remedy for rheumatism, rheumatic fever and similar ailments or that it possesses substantial curative value in the treatment of such conditions and that it is entirely safe and harmless. Back in 1919 another federal agency, the Food and Drug Administration, prosecuted the Kuhn concern for violating the original Food and Drugs Act in selling Kuhn's Rheumatic Remedy under false and fraudulent claims. Government chemists reported at that time that the nostrum was a solution of water and alcohol with potassium iodide, iodine and sugar, as well as indications of small amounts of plant material and aromatics.

Magic Shaving Powder.—This preparation, put out by the Morehouse Manufacturing Company, which traded as the Shaving Powder Company, Savannah, Ga., was advertised under various untenable claims. Among these were that "At last science has found a way to remove a beard without shaving," and readers were advised to "shave without a razor" and "merely apply Magic Shaving Powder as directed, then wipe off leaving a clear, smooth skin." The Federal Trade Commission's findings, however, were that the preparation does not constitute a new method and is not harmless in all cases, as two of the ingredients are barium sulfide and calcium hydroxide, which may be harmful to the skin and its underlying structures in persons who have tender skin, and its use may also result in injury to the eyes of careless users. On Dec. 19, 1940 the Commission ordered the Morehouse concern to cease representing that Magic Shaving Powder is a new method for removing hair or that the method prescribed for its use constitutes shaving. It also ordered the discontinuance of advertisements which fail to warn that this powder should not be used by those having a tender skin and should not be allowed to get into the eyes of users thereof.

Mayos Periodic Compound.—George D. Moorman and Roy C. Stockbridge, trading as Mayos Products Company and M. P. Company, Chicago, were ordered by the Federal Trade Commission on July 6, 1940 to cease advertising that this nostrum is a cure, remedy or competent treatment for delayed or painful menstruation or that it is harmless. Also prohibited were any advertisements which fail to reveal that the use of the product may cause serious and irreparable injury to the health of the user.

Miller's "Reducer."—This was sold under three names, "Belite," "Reducers" and "Miller's Reducing Prescription," and put out by Julius and Jessie Miller, trading as Miller Drug Company, Rochester, N. Y. They represented it as a safe, competent and effective treatment for obesity, which the Federal Trade Commission found to be false and misleading as the product contained dried thyroid in quantities sufficient to cause serious and irreparable injury to the health if used under the conditions prescribed in the advertisements or under such conditions as are customary or usual. On Dec. 16, 1940 the Commission ordered the Millers to discontinue such misrepresentations.

Quinox Capsules.—These were put out by a William S. McClymonds, trading as Oxol Laboratories and Western Research Laboratories. The concern was ordered by the Federal Trade Commission on May 6, 1940 to cease representing its product falsely as an effective treatment, cure or remedy for delayed menstruation.

Retonga.—The Retonga Medicine Company, Atlanta, Ga., was ordered by the Federal Trade Commission on July 1, 1940 to discontinue certain misrepresentations in the sale of this product. Among these were that it is a cure or remedy for diseases or disorders characterized by such symptoms or conditions as nervousness, indigestion, headaches, sluggishness, pains, poisoning, dizziness, muscular aches and pains, insomnia, biliousness, undernourishment, loss of weight or lack of strength; that it possesses any value in the treatment of these symptoms and conditions in excess of the temporary relief furnished by a mild laxative or gastric tonic when such symptoms or conditions are due to or caused by constipation or lack of appetite, or that its preparation has therapeutic value in the treatment of constipation in excess of providing temporary relief. Further representations prohibited under the order are that "Retonga" relieves the body of toxic poisons or cleanses the system; that it has any beneficial effect or therapeutic value in the treatment of kidney or bladder disorders; that it renews or restores the strength or health or has any therapeutic properties with respect to building health or strength in excess of stimulating the appetite.

Reva.—Cecil D. Kitchen, trading as the Reva Company, Chicago, was ordered by the Federal Trade Commission on July 14, 1940 to cease representing that "Reva" is not a dye or that it is anything other than a dye; that it will supply a substitute for or replace natural pigment in the hair; will restore natural or youth-like color to the hair or have any effect in stimulating its growth; that it will act as a cure or remedy for dandruff, scalp eczema or falling hair or that it is safe or harmless in treating scalp disorders.

Scholl's Foot Products.—The Scholl Manufacturing Company, Inc., Chicago, has on several occasions run afoul of the Federal Trade Commission because of unwarranted claims that were made in the advertising of its products. On Dec. 8, 1940 the Commission ordered the Scholl concern to cease and desist from certain misrepresentations in the advertising of its "Zino-Pads" and "Kurotex Foot Plasters." Among these were that the pads stop pain instantly or in one minute or make it possible to lift out corns or calluses after the application of the pads without the use of surgery or other aids; that these pads are a cure or remedy for corns, calluses or bunions, or have healing properties; that the use of the

Kurotex Foot Plasters instantly relieves the pain caused by corns, sore toes, calluses, bunions or tender spots on the feet resulting from new or tight shoes, or that they give any degree of relief from such condition beyond that which follows from the protection from outside pressure and friction or provide such relief at any time other than when they are being worn.

Sekov.—This anti-fat nostrum, also known as "Sekov Reducer," is put out by Edwin H. and Hazel Ruth Vokes, doing business as Sekov Corporation and Sekov Reducing Studios, Hollywood, Calif. On Sept. 26, 1940 the Federal Trade Commission ordered these persons and concerns to cease disseminating advertisements which failed to reveal that the use of Sekov under conditions prescribed in the advertising, or those customary or usual, may result in serious or irreparable injury to health. The findings were that the product is not, as represented, a scientific treatment for obesity when administered without a thorough medical examination and without scientific care and observation; that it does not guard the health of the user, act on a corrective principle or reduce by normalizing the body and that, contrary to such representations, the preparation does contain cathartics and dangerous drugs. The Commission further found that this nostrum constitutes a treatment for obesity only when used by persons suffering from hypothyroidism. Obesity, the findings continue, may be due to several causes, including the dysfunctioning of the pituitary gland, and to excess intake of food, in which cases the use of Sekov would be improper and ineffective. Further, the findings continue, the use of the preparation, although it may result in taking off fat by accelerating the rate of metabolism, may seriously weaken the body and its organs, including the heart, as the preparation contains a dangerous drug, an extract of thyroid.

Silver Label Formulas.—Two of these items, put out by Michael S. Chiolak, using the trade style "Tone Company," were "Silver Label Formula No. 6" and "Gold Label Formula No. 8," each known also as "Tone Periodic Compound" and sold as a remedy for delayed menstruation. On July 1, 1940 he was ordered by the Federal Trade Commission to cease circulating advertisements that failed to reveal that the use of his products may result in serious and irreparable injury to health.

Sorbol-Quadruple and Bukets.—These are put out by one Charles Keller, doing business as Sorbol Company and Keller Company, Mechanicsburg, Ohio. The city chemists of Cleveland stated years ago that they found "Sorbol-Quadruple" to be essentially soap and alcohol, with some potassium iodide. "Bukets" was once reported to contain, among other things, buchu leaves and juniper oil, common components of so-called kidney remedies. On Dec. 19, 1940 the Federal Trade Commission announced that it had ordered Keller to discontinue certain misrepresentations that had been made for these two nostrums. Among them were that Sorbol-Quadruple is a simple cure or remedy for goiter and possesses substantial therapeutic value in the treatment of that condition, and that the mixture is entirely safe and harmless; that Bukets is of any substantial value in eliminating excess acid or waste from the body, or constitutes a cure or remedy for frequent or scanty flow of urine, rheumatic pains, backache or leg pains, or possesses any substantial therapeutic value in the treatment of such conditions, or, in fact, any therapeutic value whatever in excess of its action as a mild diuretic. Keller also was ordered to discontinue any advertisements for Sorbol-Quadruple which fail to reveal that the stuff should not be used by those having tuberculosis or any form of goiter other than simple goiter (provided, however, that such advertisements need contain only a statement that the preparation should be used only as directed on the label thereof, when such label contains a warning to the effect that the preparation should not be used by those having tuberculosis or any form of goiter other than simple goiter). Still earlier (June 1937) Keller had signed a stipulation with the Federal Trade Commission agreeing to discontinue certain false and misleading representations in the sale of Bukets.

Super-Pure Laxative Bromide Quinine Tablets.—This is put out by the Spors Company of Le Center, Minn., which is run by a Frank Spors. He was ordered by the Federal Trade Commission on Oct. 17, 1940 to discontinue misrepresenting this product as a cure or remedy for colds. The Commission's findings were that it will not accomplish the results claimed, although it may afford a temporary relief for cold symptoms.

Van Vleck Nostrums.—The Dr. Van Vleck Company, Jackson, Mich., has for many years been selling by mail a combination treatment for hemorrhoids. This has included a "Dr. Van Vleck's Ointment," "Dr. Van Vleck's Muco Cones" and "Dr. Van Vleck's Pills." On May 19, 1940 the Federal Trade Commission ordered the concern to cease representing in its advertising that this treatment comprises an effective and scientific cure for hemorrhoids and that it removes them without surgical aid and insures immediate and lasting relief with no return of suffering.

Wain's Compound.—This product is put out by Wain's Laboratory, Inc., of Hollywood, Calif. It was formerly known as "Ama-Gon." On Oct. 25, 1940 the Federal Trade Commission ordered the concern to cease representing that its nostrum has any therapeutic value in the treatment of bronchial asthma or bronchial coughs in excess of furnishing temporary symptomatic relief from the paroxysms of asthma and bronchial irritations or that the preparation is in all cases safe or harmless; and to discontinue any advertisement which fails to reveal that the preparation should not be used by those having tuberculosis or goiter; provided, however, that such advertisement need contain only a statement that the preparation should be used only as directed on the label thereof, when such label contains a warning to the effect that the preparation should not be used by those having tuberculosis or goiter. More than two years earlier, on July 4, 1938, the Commission had ordered Wain's Laboratory, Inc., to discontinue representing that its product is an effective remedy or treatment for asthma, hay fever or related bronchial ailments; that it is harmless, containing no habit-forming or heart-depressing drugs and that it is a new and startling discovery.

Correspondence

LOCAL APPLICATION OF SEX HORMONES

To the Editor:—Local application of sex hormones has been attempted in occidental medicine only during the last few years. In oriental therapy evidently it was well known for centuries. The novel "The Golden Lotus" (English translation by Clemens Egerton, without date, 4 volumes, George Routledge & Sons, London; German translation by Franz Kuhn under the title Kin Ping Meh, 1 volume, without date, Inselverlag, Leipzig), by Wang Shih-Cheng, who died in 1593, gives a vivid and realistic picture of Chinese life and customs at the time of the Sung dynasty in the reign of Hui Tsung 1100-1126, with numerous medical and diagnostic as well as therapeutic details. A Hindu monk reciprocates gifts from a wealthy pharmacist by presenting him with some aphrosidiac pills to be taken "one at each occasion, no more, with a drop of spirits," and a red powder to anoint the glans penis with the advice, "every time you use it, take 2 grains and no more. Should you feel a burning sensation, take your weapon in your hand and stroke your thighs a hundred times or so. Then all will be well." The German translation of this part is more detailed and says "a little box with a red ointment, a little more than one fifth of an ounce to anoint the glans penis, sufficient for one hundred and ten applications." This means 0.0515 Gm. for one application, which indicates that it is a rather potent drug. The monk describes the effect of the remedy: "What is the merit of this medicine? . . . New strength will be given to limbs and belly, it will refresh the testicles, invigorate the penis . . . in a hundred days, hair and beard will be black once more, in a thousand days, your body will know its power. Your teeth will be stronger, your eyes more bright, your manhood made rigid. . . ."

It is interesting that fastening and fixing of teeth as a sequelae of invigoration of the testicles was mentioned by Doppler when he published the results of his rejuvenation operation by chemical sympathectomy in 1925. This he did by painting the spermatic artery with a 5 per cent phenol solution in order to achieve a long-lasting dilatation of the artery and thus hyperemia of the testicle.

Biedl, who was in favor of Doppler's operation, recommended its use and acknowledged its beneficial effect on the gingiva and teeth and recommended consideration of these changes in general as a test for rejuvenation. Possibly the monk's red ointment contained some plant extract which duplicated the effect of androgens, just as ephedrine, the extract of the root ma huang, duplicates the action of epinephrine, the adrenal hormone. This drug was used by the Chinese for a long time before it found its entrance and acceptance in occidental therapy.

One more remedy of this type may be mentioned. At the beginning of the last third of the nineteenth century the sinologist Hirth brought the root tang-kui (or kau-kiu, woen-wu, man-mo, shan-ki) to Europe, an extract of which for four and a half thousand years had been used in China in the treatment of amenorrhea and dysmenorrhea. The German pharmaceutic firm Merck in Darmstadt produced a standardized extract of this root and introduced it under the trade name Eumenol. Eumenol was used for many years as an emmenagogue in central Europe. Favorable experiences were published by Mueller, Palm, Ziemann and Popoviciu. Probably in using this drug one is dealing with another plant extract which simulates the effect of an animal hormone. Several herbal extracts of this type evidently were known to the Chinese medical profession for centuries.

Of the true animal hormones known to the Chinese, Edward H. Hume, in his recently published "The Chinese Way in Medicine," mentions only epinephrine, which, as an analysis by Chen and Jensen showed, is contained in the Chinese drug

ch'an su, the dried venom of the Chinese toad, used externally for canker sores, sinusitis and, in general, for local inflammatory conditions.

Local application of sex hormones has been used in modern occidental medicine only in 3 instances. Jadassohn and his school provoked increase in the size of the breast of the guinea pig by local application of estrogenic substance, and similar experiments were carried out by Mussio-Fournier, Albrieux and Buno, de Fremery, Lewis, Mixner and Turner. Cyril MacBryde (THE JOURNAL, March 18, 1939, p. 1045) treated women with infantile breasts by daily application of 5 grains (0.3 Gm.) of an ointment which contained estradiol or estradiol benzoate. Local application of theelin to the vagina proved an efficient therapy in gonorrhea of young girls (Lewis, Weinstein, Reichert, Epstein, Jung and Colvell) and local application to the vulva an efficient therapy in kraurosis (Foss, Buschbeck, Kaufmann).

Theoretical considerations seem to encourage the local application of sex hormones for sensitization of the organs which are the nervous receptors for sex stimulation, i. e. the glans of the penis and the clitoris. The sensitive nerves and their endings in these organs lie beneath the epithelium and are open to the sensitizing effect of the hormones, which may reach them in higher concentration when penetrating locally from the surface than when administered only by circulation of the blood. Several female patients whose clitoris was anointed two to three times a week for several weeks with estrogens showed slight enlargement of the clitoris, and women with frigidity had their normal sex desire restored. Male patients whose glans penis was treated by application of androgens recorded more frequent erections and greater persistence of erections. Clinical experiments are under way by Dr. W. M. Kearns of Milwaukee and by Dr. August F. Daro and Dr. Aaron Kanter of Chicago, and results will be published after completion.

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Chicago,

[NOTE.—Obviously the effects of psychologic and manual stimulation must be considered in evaluating these technics.—ED.]

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

CHICAGO, Feb. 16-17, 1942. Council on Medical Education and Hospitals, Sec., Dr. William D. Cutter, 535 North Dearborn Street, Chicago.

BOARDS OF MEDICAL EXAMINERS
BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, August 2, page 387.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Various centers, Sept. 10-12. Part III. Baltimore and New York City, October; Boston, November. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOGY: *Written.* Nov. 3. Final date for filing application is Sept. 23. *Oral.* Dec. 12-13. Final date for filing application is Nov. 8. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20. Final date for filing application is Sept. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written. Part I. Group B.* Various centers, Jan. 3. Final date for filing application is Oct. 6. *Oral. Part II. Groups A and B.* Atlantic City, May or June. Final date for filing application is March 1. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Chicago, Oct. 18. *Written.* March 7, 1942. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: Washington, January. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans, La.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Philadelphia, March or April, at the time of the Region I meeting of the American Academy of Pediatrics. Cleveland, May, at the time of the Region III meeting of the American Academy of Pediatrics. Los Angeles, May, at the time of the Region IV meeting of the American Academy of Pediatrics. *Written.* Locally, approximately 6 weeks in advance of the date of oral examination. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: *Oral.* New York, Dec. 19-20. Final date for filing application is Oct. 5. Sec., Dr. Walter Freeman, 1028 Connecticut Ave., N.W., Washington, D. C.

AMERICAN BOARD OF SURGERY: *Written. Part I.* Various centers, Oct. 6. Sec., Dr. J. Stewart Rodman, 225 S. Fifteenth St., Philadelphia.

AMERICAN BOARD OF UROLOGY: *Written.* Various centers, December. *Oral.* Chicago, February. Final date for filing application is Nov. 1. Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Hospitals for Profit: Right of State Labor Relations Board to Require Collective Bargaining.—The New York State Labor Relations Board applied to the supreme court, special term, Kings County, N. Y., to confirm its determination against McChesney, the respondent, who owned and operated a private hospital conducted for profit, requiring him to bargain collectively with his hospital service and maintenance employees, who had chosen a certain local of the A. F. of L. as their collective bargaining agency. The respondent questioned the jurisdiction of the Labor Relations Board over him, his hospital and his hospital employees, largely on the ground that the intent of the New York legislature in enacting the state labor relations act, which created the Labor Relations Board and gave it specified powers to prevent stated unfair labor practices, was to control labor relations in industry. His apparent contention in this connection was that "industry" was used in the labor relations act in the sense of a "recognized business activity which employs much labor and capital and is a distinct branch of trade" and that the conduct of a hospital was not an "industry" in that sense of the term. The court, however, agreed with the position of the Labor Relations Board that under the Labor Relations Act it was given jurisdiction with respect to "labor conditions in any field of employment where the objective is the earning of a livelihood on one side and the gaining of a profit on the other."

As corroborative of its views concerning the applicability of the Labor Relations Act, the court referred to *Metropolitan Life Insurance Co.* v. *New York State Labor Relations Board,* 280 N. Y. 194, 20 N. E. (2d) 390, in which the New York Court of Appeals held that the act applied to insurance agents in the New York City area, rejected the argument that the application of the act was to be confined to employees as defined in article I of the labor law, which defined employee as "Mechanic, workingman or laborer," and held that the act must be given a liberal construction to accomplish its purpose of fostering collective bargaining as between employer and employee.

Since the Labor Relations Board admitted that it had no jurisdiction over a "voluntary hospital" (apparently referring to a charitable hospital), the respondent argued that no distinction should be drawn in this respect against a hospital conducted for profit, since the functions of the two types of hospitals in the care of the sick "viewed in the sense of public need, are identical." But, answered the supreme court, judicial decision in this state has indicated a distinction between the two types of institutions. In *Jewish Hospital of Brooklyn* v. *John Doe,* 252 App. Div. 581, 300 N. Y. S. 1111 (J. A. M. A. **111**:475 [July 30] 1938), the supreme court, appellate division, second department, in holding that a statute, which was declared to be in pari materia to the Labor Relations Act, limiting the right of state courts to issue injunctions in cases involving or growing out of labor disputes did not prohibit the issue of an injunction asked for by a charitable hospital, said:

> We believe, even though the statute does not expressly exempt charitable corporations, that the Legislature never intended it to apply to an institution such as plaintiff [Jewish Hospital of Brooklyn]. While those involved in a labor dispute, as defined by the statute, need not stand in the relation of employer and employee, they must be engaged in the same "industry, trade, craft or occupation." These words connote and emphasize one common thought, to wit, that the parties to the controversy shall be engaged in the same business enterprise or commercial pursuit; one motivated by the desire for profit, the other by the desire

to earn a livelihood. . . . Obviously plaintiff is not engaged in any industry, trade, craft, or occupation for profit within the meaning of the statute.

The argument advanced by the respondent, continued the court, could be employed with equal force by a large milk corporation claiming that it performs the same function as a charitable organization devoted to the free distribution of milk. As further indicative of the correctness of this view that the Labor Relations Act applied to a private hospital conducted for profit, the court pointed out that the labor relations act specifically exempts from its provisions the employees of a charitable, educational or religious association or corporation. The court, accordingly, in effect, ordered the respondent to cease refusing to bargain collectively with the bargaining agency of his employees. On appeal to the supreme court, appellate division, second department, the order of the lower court was affirmed.—*State Labor Relations Board v. McChesney, 27 N. Y. S. (2d) 866 (N. Y., 1940) 27 N. Y. S. (2d) 870 (N. Y., 1941).*

Hospitals Not for Profit: Applicability of Minnesota State Labor Relations Act Requiring Collective Bargaining with Employees.—The Northwestern Hospital is a nonprofit, charitable corporation located in Minneapolis whose services are available to patients regardless of their ability to pay. Since the income received from pay patients is insufficient to cover its operating expenses for the continuance of its operations, it depends to a considerable extent on voluntary contributions from the public at large. In 1937 a few of its 125 maintenance and nonprofessional employees, such as janitors, laundrymen, firemen and elevator operators, were organized and joined a certain local union. Thereafter the union sought recognition as the bargaining agent of all maintenance and nonprofessional employees, and when the hospital refused to negotiate the union in May 1939 appealed to the state labor conciliator, who under the Minnesota State Labor Relations Act is given certain powers to prevent stated "unfair labor practices," included in which is a refusal to bargain collectively with employees. The conciliator, acting in pursuance to authority purportedly granted by that act, referred the dispute to the governor as one involving the public interest, and a commission representing labor, the hospital and the public was appointed. The commission reported in June 1939 that the hospital was subject to the State Labor Relations Act and the attorney general of the state concurred in that conclusion. The hospital still refused to negotiate. In February 1940 a "bannering" and picketing campaign was instituted, in the words of the court, "to inform the public that 'This hospital refuses to deal collectively with the union of its employees.'" Alleging that these acts caused unrest among its employees and generated nervousness among patients, who feared that windows would be smashed, heat and light turned off and visitors prevented from entering the hospital, the hospital sued to enjoin the union and others from picketing and "bannering." The trial court issued a temporary injunction which it later dissolved, and the hospital appealed to the Supreme Court of Minnesota.

The principal question to be determined, said the Supreme Court, is whether or not the hospital, by reason of the fact that it is a nonprofit, charitable corporation, is exempt from the provisions of the State Labor Relations Act. If it is, the action of the trial court in dissolving the injunction was erroneous. As indicative of the persons to whom the Labor Relations Act applies, the court quoted the definitions of "employer" and "employee" contained in the act, as follows:

"(b) 'Employer' includes all persons employing others . . . but does not include the state or any political or governmental subdivision thereof, nor any person subject to the Federal Railway Labor Act, . . .

"(c) 'Employee' includes, in addition to the accepted definition of the word, any employee whose work has ceased because of any unfair labor practice . . . but does not include any individual employed in agricultural labor or by his parent or spouse or in domestic service of any person at this own home." (3 Mason Minn. St. 1940 Supp., Sec. 4254-21.)

There can be no doubt, continued the Supreme Court, that both definitions are so comprehensive that they force the conclusion that a nonprofit, charitable corporation operating a hospital is within the act as one "employing others." Equally certain it is that one employed, for instance, as an elevator operator, as a janitor or in a similar occupation is an "employee" within the accepted meaning of that term. It is to be noted that while the Labor Relations Act contains certain specific exemptions, there is no exemption in favor of charitable hospitals or of their employees. The most practical inference from this fact is that the legislature specified all the exemptions it intended and that since a hospital and its employees were not specifically excluded the legislature intended that the act apply to them. Furthermore, said the court, the hospital is not "the state or any political or governmental subdivision thereof," which is expressly excluded from the definition of "employer" already given. It is true that in *Jewish Hospital of Brooklyn* v. *Doe*, 252 App. Div. 581, 300 N. Y. S. 1111; and *Western Pennsylvania Hospital* v. *Lichliter*, Ct. of Common Pleas, July 29, 1940 (Decision affirmed by the Supreme Court of Pennsylvania, 17 A. (2d) 206), the hospitals involved were held to be covered by a similar exclusionary clause contained in the definition of "employer" within the meaning of the labor relations acts of the states involved, but in both of those cases the hospitals involved received public funds for caring for patients to whom the particular governmental subdivision owed a duty to provide. Here the relation between the plaintiff hospital and the state is not sufficient to classify the hospital as an agency of the state.

The Supreme Court thought the intent of the legislature to make a hospital such as the plaintiff amenable to the Labor Relations Act was also clearly evidenced in that section of the act (Sec. 4254-27) that provides that—

"If the dispute is in any industry, business *or institution* affected with a public interest, which includes, but is not restricted to, any industry, business *or institution* engaged in supplying the necessities of life, safety, or health, so that a temporary suspension of its operation would endanger the life, safety, health or well-being of a substantial number of people of any community," the labor conciliator shall notify the Governor, who may appoint a commission of three to conduct a hearing and make a report.

It will be noted, said the Supreme Court, that in this provision, in addition to the inclusion of industry and business, an "institution" is specifically incorporated. Obviously the reference cannot be to a state institution since such an institution is exempted from the act, because, as previously noted, "the state or any political subdivision thereof" is specifically excluded from the definition of an "employer" subject to the act. The word "institution" then, as here used, must be taken in its ordinary sense. A hospital such as the plaintiff hospital is generally regarded as an institution in the community. It is not a business or industry but it is concerned with the well-being of the people. The intention of the legislature is more evident when consideration is given to the provision relating to the suspension of activity being a peril to a substantial number of people. It seems apparent that just such a situation as is now before us was contemplated by this statute. There is a clear recognition that hospitals are within the act.

While it is true, continued the court, that ordinarily labor legislation has been concerned principally with industrial labor relations, to place such a restricted meaning on the Labor Relations Act would amount to judicial legislation instead of interpretation. The employer-employee problem is more far reaching and to impute to the legislature a purpose to provide means for the adjustment of labor relations in industry only would be artificial. The duties of thousands of hospital employees are similar to those of employees in private industry. The position and rights of employees in a hospital are as important to the well-being of the whole community as those of technical industrial employees. The simple fact is that employees are dependent on their positions for livelihood. This is true whether the employer is a charitable hospital or an automobile manufacturer. The Labor Relations Act does not make the right to bargain collectively dependent on the nature of the employer's operation. Since the act is clear and unambiguous, there is nothing for us to construe. While it is true that the preamble of the Labor Relations Act reads: "An act relating to the avoidance and settlement of labor disputes and the promotion of industrial peace . . ." the fact is that the enactment itself goes beyond "industrial peace" but deals with "labor disputes" in institutions concerned with health and safety of a substantial number of people.

In view of the clarity of the statute, the court refused to give weight to the New York and Pennsylvania decisions referred to in which nonprofit, charitable hospitals were held not to be within the Labor Relations Acts of those states. The court accordingly affirmed the action of the lower court in dismissing the injunction restraining the defendants from picketing or "bannering." In a special concurring decision, Stone, Justice, while agreeing in the result reached by the court, could not to be within the labor relations acts of those states. The elsewhere that the maintenance and nonprofessional employees of a general hospital are not engaged in 'industry' within the meaning of the applicable statutes."—*Northwestern Hospital, Minneapolis, Minn., v. Public Building Service Employes' Union Local No. 113, 294 N. W. 215 (Minn., 1940).*

Hospitals Not for Profit: Pennsylvania State Labor Relations Act Requiring Collective Bargaining with Employees Not Applicable.—The twenty-five hospitals concerned in the present action are all nonprofit, charitable institutions. Twenty-one of them rendered in 1938 free services to the indigent at a cost of $2,390,000 for which they received state contributions amounting to $665,000. The difference was "made up from charitable contributions. For the fiscal year ending May 31, 1939, excluding one hospital, there was an operating deficit for the plaintiff hospitals of $464,000, and of the twenty-five hospitals involved only six failed to show deficits."

The defendant union attempted to unionize the maintenance and nonprofessional employees of these hospitals and made certain demands, but the hospitals refused to negotiate with the union. The union then filed a petition with the Pennsylvania Labor Relations Board, which under the Pennsylvania State Labor Relations Act is given certain powers to prevent stated "unfair labor practices," included among which is a refusal to bargain collectively with employees. The hospitals filed a bill in equity with the court of common pleas, Dauphin County, Pa., to enjoin the board from proceeding against them under the Labor Relations Act and to enjoin the union from asserting rights against them purportedly granted by the act. The bill alleged that the hospitals concerned were not within the purview of the Labor Relations Act because (1) the provisions of the Labor Relations Act apply only to labor disputes in industry, commerce, trade, business or production and they are not engaged in such activities and (2) in performing the services they do they are performing a governmental function and governmental agencies are expressly exempted from the provisions of the act. The trial court issued a preliminary injunction without a hearing and the Labor Relations Board and the union appealed to the Supreme Court of Pennsylvania, which affirmed the action of the trial court and adopted its opinion.

The first question presented was whether or not the trial court had jurisdiction to issue an injunction without a hearing. The Pennsylvania Labor Anti-Injunction Act provides, in part, that in a case involving a labor dispute a court shall not have the authority to issue a preliminary injunction without affording a hearing to both the plaintiff and the defendant. Section 3 (*a*) of that act (1937, P. L. 1198; 1939 P. L. 302) provides that:

> A case shall be held to involve or to grow out of a labor dispute when the case involves persons who are engaged in a single industry, trade, craft, or occupation. . . .

A hospital, said the court, is not an industry. Neither are the employes of a hospital engaged in a single trade, craft or occupation. The employees of a hospital may have a common employer but they have no single trade, craft or occupation. Giving the words "industry, trade, craft or occupation" their commonly accepted meaning, we feel that they do not include the operations of a hospital. Even though the words of the statute are interpreted as broad enough to include the operations of a hospital, we do not think that the legislature intended such a result. The purpose of the act is to preserve the status quo during labor disputes, to insure the right to bargain collectively and to give to employees the right to choose representatives for this purpose. To show the scope of the act, the legislature attempted to define cases which "involve or . . . grow out of a labor dispute." In doing so, it used the words "industry, trade, craft or occupation." It has not been the custom in the past to unionize hospitals. The effect of unionization and attendant efforts to enforce demands would involve results far more sweeping and drastic than mere property rights. The question of profits for the employer or wages for the employee are not alone involved. It is not merely a matter of suspending operations, ceasing work and stopping production, such as might be true in a steel mill or automobile factory. It is a question of protecting the health, safety and, in many cases, the very lives of those persons who need the service a hospital is organized to render. The results are quite different and more extensive than are those involved in an ordinary labor dispute. We cannot conceive that the legislature intended to include hospitals within the purview of the act. Consequently, even though the words used might conceivably be broad enough to include a hospital, nevertheless, a hospital is not within the spirit of the act and, not being within the spirit, the act does not apply to it. As authority for the last statement the court quoted from the opinion of the United States Supreme Court in *Holy Trinity Church* v. *United States,* 143 U. S. 457, 12 S. Ct. 511, as follows:

> It is a familiar rule that a thing may be within the letter of the statute and yet not within the statute, because not within its spirit nor within the intention of its makers. This has been often asserted, and the Reports are full of cases illustrating its application. This is not the substitution of the will of the judge for that of the legislator; for frequently words of general meaning are used in a statute, words broad enough to include an act in question, and yet a consideration of the whole legislation, or of the circumstances surrounding its enactment, or of the absurd results which follow from giving such broad meaning to the words, makes it unreasonable to believe that the legislator intended to include the particular act.

We are convinced, continued the court, not only that the labor anti-injunction act has no application to a hospital but also that the effects of holding to the contrary would be so dangerous, disastrous and absurd as not to be within the intent of the legislature. The court accordingly held that nothing in the Labor Anti-Injunction Act legally deprived the trial court of the power to issue the preliminary injunction before the hearing.

The next question before the court was whether or not there was anything in the Pennsylvania Labor Relations Act which deprived the court of the power to issue the preliminary injunction. The Labor Relations Act was designed "to protect the right of employees to organize and bargain collectively." A labor relations board was created to carry out the provisions of the act. Within the scope of its authority this board initially exercises certain powers. With these the courts have nothing to do until resort is had to them for aid in enforcing orders, or in cases of appeal. But the present question is whether the plaintiff hospitals are employers within the meaning of the Labor Relations Act. The court again adverted to the Holy Trinity Church case, supra. In that an act of Congress was involved which made it unlawful to prepay the transportation of any alien into the United States under any contract or agreement made previous to migration to perform service of any kind in the United States. The church made a contract with an alien preacher to serve as its pastor. The act was held not to apply to those circumstances, the Supreme Court conceding that while the literal reading of the statute included the contract of the alien preacher, the statute was never intended to apply to such a case. Hospitals, said the court, are scientific institutions created for a humane purpose in amelioration of the sufferings of mankind. They require for their successful operation highly skilled physicians, surgeons, technicians, experts and nurses. They likewise require the services of other persons, some of whom may be skilled and some unskilled. But the whole must be coordinated, controlled and uninterrupted to accomplish the general purpose. This would be impossible should the Labor Relations Act be held applicable with all its attending ramifications, interruptions and possible cessation of service due to labor disputes and attending financial inability to function. Surely the legislature had no such intention, and we cannot so find in the absence of a clear and positive declaration to that effect.

As additional grounds for its holding the court referred to the fact that the word "employer," as defined in the Labor Relations Act, excludes the commonwealth or any political subdivision thereof. Of course, said the court, the plaintiff hospitals are not political subdivisions of the commonwealth. They are, however, with few exceptions, agencies selected by the commonwealth as a means of assisting in some degree the

indigent sick, disabled, injured or afflicted. Should the state choose to operate general hospitals, as it does certain mental hospitals, no one would claim that it was not performing a function of government and in so doing is not an employer within the meaning of the Labor Relations Act. Since the state chooses to perform this function through agencies supported in part by state appropriations, these agencies are likewise beyond the scope of the act. Were this not so, the appropriations might be diverted from their intended purpose to aid the indigent sick and injured to the payment of wages and increased operating costs. We think it obvious and indisputable that hospitals of this character are impressed with a public interest which takes them out of the purview of the act.

It was accordingly concluded that the trial court had the power to grant the preliminary injunction. Subsequently on June 9 and 11, 1941, the trial court issued a permanent injunction against the defendants perpetually restraining them and their successors, in the case of the defendant Labor Relations Board, from asserting any jurisdiction under the Labor Relations Act with respect to the plaintiff hospitals and, in the case of the union defendants, from asserting any rights against these hospitals under that act.—*Western Pennsylvania Hospital et al. v. Lichliter, 17 A. (2d) 206 (Penna., 1941).*

Workmen's Compensation Acts: Medical Testimony that Cerebral Thrombosis Possibly Resulted from Infected Thumb Not Sufficient for Award.—In the course of his employment, April 9, Burton, a man aged 61, in good health and with no observable "material hardening of arteries," ran a sliver in his left thumb. An infection developed and he went to a physician about a week later. In the opinion of the physician, the infection was localized, "did not go into his system" and, although serious so far as the function of the thumb was concerned, was not serious so far as his system was concerned. The thumb healed "perfectly well" but "continued to be more tender than the other thumb," owing to scar tissue and the recent inflammation. Toward the end of May the physician was called in to attend Burton and found that he had difficulty in walking, "had been a bit confused, was unable to get about his house without some help and was in a weakened condition." The patient was taken to a hospital where he died three weeks later of cerebral thrombosis. Attributing a causal relation between the industrial accident and the death, Burton's widow instituted proceedings under the workmen's compensation act of Vermont and was awarded compensation by the commissioner of industrial relations. The employer and his insurance carrier appealed to the Supreme Court of Vermont, Windham.

At the hearing before the commissioner, the only medical evidence tending to indicate a causal relation between the industrial accident and the thrombosis was the testimony of the attending physician that in his opinion the infection could have been a possible contributing cause of the thrombosis. This, the employer and his insurance carrier contended, was not legally sufficient to support the finding that the injury to the thumb resulted in death. Where, said the Supreme Court of Vermont, the evidence adduced in any particular case is such that any layman of average intelligence would know, from his own knowledge and experience, that the injuries involved in that case are the cause of death, expert evidence is not necessary to establish the causal relationship between the injury and the death. But where, as here, the physical processes terminating in death are obscure and abstruse and concerning which a layman can have no well founded knowledge and can do no more than indulge in mere speculation, without expert medical testimony the trier cannot properly find a causal relation. In this case, the mere fact that the infection in Burton's thumb resulting from the sliver could have been a possible contributing cause of his death does not alone warrant a finding that it was. There must be created in the mind of the trier something more than a possibility, suspicion or surmise that such was the cause, and the inference from the facts proved must be at least the more probable hypothesis, with reference to the possibility of other hypotheses. The commissioner recognized that the cause of death was obscure, that expert medical testimony could alone lay a foundation for his award and that the testimony of the physician that the infection from the sliver could have been a possible contributing cause of death, without more, was not enough to support an award. But by taking into consideration all the evidence, not only the expert testimony but also all the circumstances of the case as shown by the evidence, he concluded that he was justified in finding that the sliver was the cause of death. Since expert evidence that an accident can or cannot cause a certain result may affect the conclusion to be reached, it follows that in the case of injuries so naturally and directly connected with the accident that proof of causation does not depend on expert evidence, medical testimony of "possibility" may corroborate the other testimony. But unless the facts, outside such medical testimony, fairly warrant the conclusion that the injury resulted from the accident, causation is not established. A possible cause cannot be accepted as the operating cause unless the evidence excludes all other causes or shows something in direct connection with the occurrence.

The widow claimed that medical evidence of "possibility" is sufficient to lay the medical foundation necessary to justify a finding of causal relationship when considered with the other evidence of a lay nature. The court then discussed three Massachusetts cases which were cited in support of this proposition. These cases, the court concluded, announced a proposition that medical evidence of "possibility" may make an otherwise insufficient proof of causation sufficient. Except on such a theory, said the court, the commissioner's conclusion cannot be sustained. However, we cannot endorse such a proposition where the evidence does not bar all other causes. Unless the other evidence fairly warrants a finding of causation or excludes all other causes, a conclusion based on medical evidence of "possibility" would be entirely speculative. Here we are simply told that the infection in the thumb could possibly have caused the cerebral thrombosis, which was the immediate cause of death. There is no testimony as to what cerebral thrombosis consists of, or what causes it or if it has any relationship to hardening of the arteries. In spite of Burton's good health so soon before his death, a layman of average intelligence, from his own knowledge and experience, could have no well grounded knowledge that the sliver was the cause of death. Although the sliver might have caused the fatal illness, the trier could only speculate as to whether it did or not.

For the reasons stated, the court annulled and set aside the order of the commissioner awarding compensation.—*Burton v. Holden & Martin Lumber Co., 20 A. (2d) 99 (Vt., 1941).*

Society Proceedings

COMING MEETINGS

American Association for the Study of Neoplastic Diseases, Washington, D. C., Sept. 4-6. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.

American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Hot Springs, Va., Sept. 11-13. Dr. James R. Bloss, 418 Eleventh St., Huntington, W. Va., Secretary.

American Association of Railway Surgeons, Chicago, Sept. 8-10. Dr. Daniel B. Moss, 547 West Jackson Blvd., Chicago, Secretary.

American Congress of Physical Therapy, Washington, D. C., Sept. 1-5. Dr. Richard Kovacs, 2 East 88th St., New York, Secretary.

American Hospital Association, Atlantic City, N. J., Sept. 15-19. Dr. Bert W. Caldwell, 18 East Division St., Chicago, Executive Secretary.

American Roentgen Ray Society, Cincinnati, Sept. 23-26. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Canada, Secretary.

Colorado State Medical Society, Estes Park, Sept. 17-20. Mr. Harvey T. Sethman, 537 Republic Bldg., Denver, Executive Secretary.

Indiana State Medical Association, Indianapolis, Sept. 23-25. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Kentucky State Medical Association, Louisville, Sept. 29-Oct. 3. Dr. Arthur T. McCormack, 620 South Third St., Louisville, Secretary.

Michigan State Medical Society, Grand Rapids, Sept. 16-18. Dr. L. Fernald Foster, 2020 Olds Tower, Lansing, Secretary.

Mississippi Valley Medical Society, Cedar Rapids, Iowa, Oct. 1-3. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

National Medical Association, Chicago, Aug. 18-22. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.

Nevada State Medical Association, Elko, Sept. 26-27. Dr. Horace J. Brown, P. O. Box 698, Reno, Secretary.

Northern Minnesota Medical Association, St. Cloud, Aug. 15-16. Dr. Clarence Jacobson, Chisholm, Secretary.

Oregon State Medical Society, Portland, Sept. 3-6. Dr. M. L. Bridgeman, 1020 S. W. Taylor St., Portland, Secretary.

Rocky Mountain Medical Conference, Yellowstone Park, Wyo., Sept. 2-4. Mr. W. H. Tibbals, 610 McIntyre Bldg., Salt Lake City, Secretary.

Washington State Medical Association, Seattle, Aug. 24-26. Dr. Vernon W. Spickard, 1305 Fourth Ave., Seattle, Secretary.

Wisconsin, State Medical Society of, Madison, Sept. 10-12. Mr. G. B. Larson, 110 East Main St., Madison, Assistant Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1931 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

10:353-396 (May) 1941

Hyperthyroidism in Elderly Patients. D. H. Poer, Atlanta, Ga.—p. 353.
Nutritional Deficiencies as Public Health Problem in Alabama. J. N. Baker, Montgomery.—p. 358.
Surgical Management of Goiter. J. D. Wilson, Birmingham.—p. 363.
Some Ailments Peculiar to Infancy and Childhood: Their Cause and Prevention. J. C. Johnson, Hamilton.—p. 365.
Treatment of Common Proctologic Conditions. N. L. Andrews, Birmingham.—p. 368.
Burch Vaginal Operation for Sterilization. C. Johnson, Montgomery.—p. 370.

American Heart Journal, St. Louis

21:545-688 (May) 1941

Prophylaxis Against Lethal Effect of High Altitude by Means of Digitalis Glycoside (Gitalin). E. Fischer, Richmond, Va.—p. 545.
Low Voltage of QRS Waves in Electrocardiogram, with Especial Reference to Lead IV. C. E. Leach, W. C. Reed and P. D. White, Boston.—p. 551.
Continuous Vasodilatation in Extremities Produced Reflexly: Physiologic Studies on Temperature of Skin and on Volume Flow of Blood. G. E. Brown Jr. and E. V. Allen, Rochester, Minn.—p. 564.
Auriculoventricular Ratio and Its Relationship to Electrical Axis of Heart. A. H. Clagett Jr., Providence, R. I.—p. 574.
*Livedo Reticularis: Peripheral Arteriolar Disease. N. W. Barker, E. A. Hines Jr. and W. M. Craig, Rochester, Minn.—p. 592.
Observations on Pathologic Effects of Thiocyanate: Experimental Study. H. A. Lindberg, M. H. Wald and M. H. Barker, Chicago.—p. 605.
Quantitative Changes in Capillary-Muscle Relationship in Human Hearts During Normal Growth and Hypertrophy. J. T. Roberts and J. T. Wearn, with technical assistance of Irene Boten, Cleveland.—p. 617.
*"Anoxemia Test" in Diagnosis of Coronary Insufficiency. R. L. Levy, N. E. Williams, H. G. Bruenn and H. A. Carr, New York.—p. 634.
Experimental Atherosclerosis: III. Electrocardiographic Studies and Pathologic Changes in Hearts of Cholesterol-Fed Rabbits. Jan Nyboer, M. Bruger and S. M. Rabson, New York.—p. 657.
New Clamp for Gradual Occlusion of Coronary Arteries. K. R. Phelps, Cleveland.—p. 664.

Livedo Reticularis.—Barker and his collaborators report 13 cases of livedo reticularis or peripheral vascular disease. All the patients presented a persistent bluish red mottling of the skin of legs and feet. The mottling extended to the thighs in a few; it involved hands and arms to a less degree, and occasionally the lower part of the trunk. The livedo became more noticeable on exposure to cold, and there was a persistently lowered cutaneous temperature. The age at onset varied from 21 to 47 years. There was no evidence of syphilis, tuberculosis, tuberculids, occlusive disease of the larger arteries, varicose veins or venous insufficiency. Three patients had recurring ulceration of the skin of the legs. This, they stated, began as an intensification of an area of bluish discoloration. The ulcers of 2 were resistant to treatment and all were extremely painful. In the patient with the most extensive ulceration, occlusion of the arteries of each great toe developed on separate occasions. Three patients had a peculiar type of gangrene of the skin of the toes which persisted for several weeks or months and involved the distal half of the toes. In each instance the skin ultimately became black and hard and finally sloughed with healing except in 1, for whom amputation became necessary because of nonhealing and severe pain. A common etiologic factor could not be demonstrated. The clinical manifestations differed distinctly from Raynaud's disease, acrocyanosis or thromboangiitis obliterans. The available data indicate that in livedo reticularis there are usually organic changes in the arterioles of the skin, with chronic vasospasm, which result in regional atony and dilatation of capillaries and slowing of the blood flow. Lumbar sympathetic ganglionectomy performed in two cases definitely improved the circulation and prevented further attacks of gangrene. It was unsuccessful in 1. Sympathectomy seems a justifiable procedure when no definite etiologic factor can be found and superficial gangrene is present.

Anoxemia Test.—Levy and his co-workers performed 326 anoxemia tests on 115 normal persons and 147 patients with suspected or manifest heart disease. During the course of the tests 2,316 electrocardiograms were made. In normal persons the electrocardiographic changes during anoxemia are relatively slight. Usually the amplitude of T waves in all of the four leads is lowered, and the T wave in leads 2 and 3 may be inverted. The established criteria for an abnormal response are sufficiently rigid to exclude alterations in the electrocardiogram resulting from emotion or other spontaneous variables. The test was positive in 18 per cent of 33 patients with suspected coronary sclerosis, in 31 per cent of 22 patients with coronary sclerosis but no history of anginal attacks, in 55 per cent of 73 patients with coronary sclerosis and a history of anginal attacks and in 5 per cent of 19 patients with hypertension without coronary sclerosis. The highest incidence of positive tests occurred among 49 patients with anginal pain caused by coronary sclerosis; an abnormal response was obtained in 69 per cent. There was no relationship between the incidence of positive tests, the size of the heart and the degree of pain during anoxemia. There was no constant effect on pulse rate and blood pressure. Seventeen patients experienced twenty-four reactions: vasovagal attacks, convulsions, hyperventilation, dyspnea and mental confusion. None of them were serious or harmful. There were 9 deaths at varying intervals after the test. A negative test does not rule out the possibility of early coronary lesions or healed cardiac infarction. The test when positive is a sign of coronary insufficiency and indicates a diminished coronary reserve. It has proved of value in distinguishing pain of coronary origin from that due to other causes. It gives a graphic record of the efficiency of coronary circulation at varying intervals following coronary occlusion. The effect of various drugs on the coronary circulation can be determined. It is suggested that it may be used to measure the effectiveness of establishing collaterals in the coronary bed following surgical operations designed to promote their formation. It may prove useful when disability is claimed because of anginal pain and in insurance examinations when coronary sclerosis is suspected. Only a positive result should be regarded as significant.

American Journal of Diseases of Children, Chicago

61:915-1130 (May) 1941

Evolution of Hemiplegias in Infancy. R. K. Byers, Boston.—p. 915.
Vascular Anomalies of Spinal Cord in Children. D. N. Buchanan and A. E. Walker, Chicago.—p. 928.
Development of Fetal Lung, with Special Reference to Lining of Alveoli and Effect of Immaturity on Respiration. R. F. Norris, Philadelphia; T. T. Kochenderfer, Norristown, Pa., and R. M. Tyson, Philadelphia.—p. 933.
Effect of Pubertas Praecox on Age at Which Onset of Walking Occurs. W. Dennis, University, Va.—p. 951.
Hyperbilirubinemia in the Newborn. L. T. Davidson, Katharine K. Merritt and A. A. Weech, New York.—p. 958.
Phosphorus Retention in Children with Chronic Renal Insufficiency: Effect of Diet and of Ingestion of Aluminum Hydroxide. S. Freeman and Willie Mae Clifton Freeman, Chicago.—p. 981.
*Character of Congestive Failure in Children with Active Rheumatic Fever. B. J. Walsh, Washington, D. C., and H. B. Sprague, Boston.—p. 1003.
*Hypertension Associated with Unilateral Chronic Atrophic Pyelonephritis: Occurrence in Child in Whom No Decrease of Blood Pressure Followed Nephrectomy. B. Benjamin and M. Ratner, Montreal, Canada.—p. 1051.

Rheumatic Fever and Congestive Failure.—Walsh and Sprague describe clinical features of congestive failure in children with rheumatic heart disease. Their observations are based on a study of 44 children from 3 to 15 years of age seen at the House of the Good Samaritan between July 1937 and April 1940. The initial signs of heart failure were enlargement of the liver and puffiness of the face accompanied by an unexpected gain in weight. A few children with congestive failure and active rheumatic fever preferred to lie flat in bed. These

children had pronounced puffiness of the face, which caused them to look as if they had primary renal disease. Pulmonary rales were seldom heard; their appearance was limited to the terminal stages of the illness. Other important evidences were high venous pressure apparent at the onset of the failure, a shift of the electrical axis of the heart to the right, which increased with progression of the heart failure and decreased or disappeared with the patient's improvement or recovery, and a well defined diastolic gallop rhythm along the upper left sternal border.

Hypertension and Atrophic Pyelonephritis.—Benjamin and Ratner present the case of a boy of 6 with hypertension associated with pronounced atrophic pyelonephritis and severe functional impairment of one kidney but with no evidence of any other abnormality. He was subjected to a nephrectomy, after which there was no decline of the systolic or the diastolic blood pressures immediately and for the following six months. The principal pathologic features consisted of extensive fibrosis, decided diminution of the normal renal tissue and thickening of the arterioles in the fibrotic regions, a picture similar to that of unilateral chronic pyelonephritis associated with elevated blood pressure which decreases after nephrectomy. The relation between hypertension and renal disease requires further elucidation. At present it appears impossible to formulate definite criteria for selecting cases of unilateral nephropathy and hypertension in which a reduction in blood pressure may be expected to follow nephrectomy. A urologic examination is indicated in any child with chronic hypertension associated with renal disease. If such an examination demonstrates the presence of a unilateral renal lesion and operation is not contraindicated, nephrectomy may be justified. The hypertension may disappear after the operation, but that such a result may not follow should also be borne in mind.

American Journal of Ophthalmology, Cincinnati

24:485-610 (May) 1941

Fifty Years' Experience in Ocular Motility: Part I. W. B. Lancaster, Boston.—p. 485.

Orbital Tumors and Their Surgical Treatment: Part II. A. B. Reese, New York.—p. 497.

Monocular Diplopia: Report of Case. M. H. Pincus, Brooklyn.—p. 503.

Scotoma Associated with Menstruation. J. N. Evans, Brooklyn.—p. 507.

Removal of Lens in High Myopia in Which Lenticular Opacities Prevent Improvement of Vision by Correcting Lenses. B. Chance, Philadelphia. p. 519.

Exophthalmos in Hyperthyroidism. D. Kravitz and W. V. Moehle, Brooklyn.—p. 527.

Retinal Teletraumatism: Traumatic Retinal Angiopathy (Purtscher). J. W. Smith, New York.—p. 537.

Preservation of Convergence with Paralysis of All Lateral Movements in Case of Intramedullary Tumor of Pons. W. S. Reese and J. C. Yaskin, Philadelphia.—p. 544.

American Journal of Physiology, Baltimore

133:1-188 (May) 1941. **Partial Index**

Part Played by Carotid Body Reflexes in Respiratory Response of Dog to Anoxemia With and Without Simultaneous Hypercapnia. P. R. Dumke, C. F. Schmidt and H. P. Chiodi, Philadelphia.—p. 1.

Effect of Vasoconstrictor Substances in Shed Blood on Perfused Organs. R. J. Bing, with assistance of B. Gallardo, New York.—p. 21.

Nutritional Value of Some Common Carbohydrates, Fats and Proteins Studied in Rats by Single Food Choice Method. C. P. Richter, Baltimore.—p. 29.

Lymph Drainage of Gallbladder Together with Observations on Composition of Liver Lymph. Jane D. McCarrell, Sylvia Thayer and C. K. Drinker, Boston.—p. 79.

Concentration of Ascorbic Acid and Phosphatases in Secretions of Male Genital Tract. O. C. Berg, C. Huggins and C. V. Hodges, Chicago. —p. 82.

Study of Gaseous Exchange Between Circulatory System and Lungs. N. Underwood and J. T. Diaz, Nashville, Tenn.—p. 88.

Seasonal and Postural Changes in Blood Volume Determined by Carbon Monoxide Method, Employing Differential Electric Photometer for Estimation of Low Percentage Saturations of Hemoglobin with Carbon Monoxide. M. E. Maxfield, H. C. Bazett and C. C. Chambers, Philadelphia.—p. 128.

Papaverine Hydrochloride and Ventricular Fibrillation. E. Lindner and L. N. Katz, Chicago.—p. 155.

Effects of Training and of Gelatin on Certain Factors Which Limit Muscular Work. S. Robinson and P. M. Harmon, with technical assistance of E. S. Turrell and F. O. Mackel, Bloomington, Ind.—p. 161.

Effects of Carbon Monoxide Anoxemia on Flow and Composition of Cervical Lymph. F. W. Maurer, Boston.—p. 170.

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American Journal of Public Health, New York

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Disabling Sickness Among Industrial Workers, with Particular Reference to Time Changes in Duration. W. M. Gafafer, Washington, D. C.—p. 443.

Use of Culture Method in Clinical Management of Gonorrhea. G. Sewell, Emilie Clarke and E. Nelson, Detroit.—p. 457.

Place of Maternal and Child Health Services in Generalized Program in a Health Unit. W. J. French, Annapolis, Md.—p. 465.

A County Health Unit with Proper Functioning Maternal and Child Health Program. I. Dyer, Tahlequah, Okla.—p. 471.

Medical and Dental Services for Dependent Children Under Public and Private Child Caring Agencies. L. C. Cole, Cleveland.—p. 477.

Proposed Method for Bacteriologic Examination of Flat Surfaces. W. G. Walter and G. J. Hucker, Geneva, N. Y.—p. 487.

Enforcement of Dishwashing: Regulations Applying to Eating and Drinking Establishments. W. von D. Tiedeman, Albany, N. Y.—p. 491.

Selection, Training and Supervision of County Sanitarians in West Virginia. J. B. Baker, H. K. Gidley and G. L. Kelso, Charleston, W. Va.—p. 498.

American Journal of Surgery, New York

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*Conservatism in Gastric Surgery: New Technic for Resection. J. L. De Courcy, Cincinnati.—p. 200.

Distribution of Anesthesia Following Block of Sacral Nerves. G. E. Burford, New York, and L. A. Watkins, Leavenworth, Kan.—p. 206.

Analysis of 151 Cases of Intussusception from Charity Hospital of Louisiana at New Orleans. H. R. Kahle, New Orleans.—p. 215.

*Reduced Temperatures in Surgery: I. Surgery of Limbs. F. M. Allen, New York.—p. 225.

Open Surgical Reduction of Fracture Dislocation of Lumbar Spine with Cord or Cauda Equina Involvement. C. G. Barber, Cleveland.—p. 238.

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Carcinoma of Ampulla of Vater: Three Cases of Transduodenal Resection. L. River, R. W. McNealy and A. B. Ragins, Chicago.—p. 289.

Causalgic Backache. O. C. Hudson, C. A. Hettesheimer and P. A. Robin, Hempstead, N. Y.—p. 297.

Factors in Etiology of Chronic Noncalculous Cholecystitis. M. J. Brown, Davenport, Iowa.—p. 304.

Use of Stilbestrol in Menopause and Other Conditions. L. Kurzrok, C. S. Birnberg and H. Weber, Brooklyn.—p. 311.

Diverticula of Stomach. H. W. Schmidt and W. Walters, Rochester, Minn.—p. 315.

Bursa and Ganglion. J. H. Cherry and R. K. Ghormley, Rochester, Minn.—p. 319.

Conservatism in Gastric Surgery.—De Courcy operated on patients with gastric and duodenal ulcers and cancer in two stages in an effort to reduce the mortality. The procedure has been followed in his clinic for the last few years. For pyloric ulcer a gastroenterostomy was done first and was followed several weeks later by resection of the ulcerative area. By this method it has been found possible, if necessary, to do a high posterior gastroenterostomy on doubtful or poor risk patients and to improve their general physical condition. Usually within a short time they were able to withstand the actual removal of the ulcerous or cancerous area, which would probably have proved fatal if it had been undertaken at the outset. The two stage operation thus offers an excellent chance of success in cases in which the more radical procedures would not be feasible. By doing this operation when the disease is still in a relatively early stage, the patient's strength is conserved and he is fitted for the strain of the actual resection. The mortality has been reduced to less than 10 per cent. It has been the experience at the clinic that patients with ulcer need psychologic as well as physical supervision. The importance of the mental as opposed to the physical disturbance which the sufferer from gastric lesions endures is nearly equal to the physical handicaps. The author does not regard the two stage procedure as universally applicable. Its advantages, especially in carcinoma of the pylorus, are that it obviates retraction of the esophagus and that there is much less danger of contamination when the preliminary gastroenterostomy is employed. In ulcer cases there is always the possibility that resection may be avoided altogether, as the ulcer will sometimes heal when the irritation of the passage of material impregnated

with digestive juices is eliminated. The author believes that his technic of stomach resection presents less likelihood of immediate and remote complications. He begins the resection at the upper or proximal portion of the stomach, so that the area to be excised is removed from above downward. This makes it possible to visualize the posterior gastric wall while the resection is being made. The proximal portion of the gastric wall is covered with a heated pad and the distal end is raised, permitting the clamping and division of the gastrocolic and gastrohepatic omentums. If adhesions are present on the posterior wall of the stomach, they are divided as far down as the attachment of the pancreas to the duodenum. At this point the attachment to the duodenum is easily stripped off as far as necessary. The duodenal arteries are divided and ligated, and the duodenum is divided in the usual manner. Anastomosis is then performed between the jejunum and the stomach. The method, the author believes, has the advantages of speed, accuracy and simplicity. In his hands it has proved preferable to the older methods.

Reduced Temperatures in Surgery.—The modification of local metabolism by temperature, according to Allen, enormously influences the survival from a few hours or even minutes at elevated temperatures to fifty-four hours at a temperature near freezing. Both primary and secondary shock are abolished by suitably low temperature. For amputations and other procedures the patient sits up with the leg immersed in ice water about 1 inch above the tourniquet. Weaker patients are allowed to lie with their heads slightly elevated and the leg or thigh placed on a layer of ice and covered completely with cracked ice. From 2 to 5 teaspoons of salt is added to the ice in each bag. Temperatures, taken by occasionally inserting an ordinary laboratory thermometer between the ice bags and the skin, around 41 F. assure adequate chilling and safety against actual freezing. For an emaciated shin one hour may suffice for through and through anesthesia, or as long as five hours may be required for a rather thick thigh. If the sciatic nerve cannot be cut at midthigh without attracting the patient's notice and with no change in pulse or blood pressure, something has been wrong in the preparation. The duration and extent of dissection are immaterial; all that matters is the condition left after completion. Shock is nonexistent except for the slight degree which may develop from tissue injury remaining after the wound is closed and the temperature is raised, allowing protoplasm to resume its functions. The limb is removed from ice bags in the operating room, is sterilized and the operation completed as usual. If solutions are to be used for sponging or other purposes they should be iced. For any particularly long operation the limb may be kept on a bed of ice bags. The cooler the operating room the better. The tourniquet is released when the wound is ready for closure. Circulation returns promptly, and bleeding points can be caught and ligated. The anesthesia continues long enough for convenient suturing. The guiding principle of postoperative care is to reduce the temperature to whatever extent may be necessary, but to raise it as fast and as far as may be safe. In cases in which there is an adequate blood supply there is no objection to letting the temperature of the stump return immediately to normal. Temperature regulation makes it possible to reduce tissue metabolism in the operated part to a level for which the existing blood supply is adequate and to maintain it at such a level until the circulation improves. The danger period of postoperative shock from damaged tissue can be bridged by temperature control. Refrigeration is applicable to conditions not handicapped by senility and arteriosclerosis, to war wounds and to industrial accidents. A large number of military and industrial wounds consist in mutilations of limbs, and to these the results of animal experiments are applicable. In warm weather ice is often available or can be specially provided. In cold weather only precautions against actual freezing are needed. Efficient chilling prevents the shock resulting from the tourniquet needed to stop hemorrhage. It also wards off local gangrene when the tourniquet is retained for a long time. The transportation of wounded persons is painless as far as limb injuries are concerned. Strength and resistance are probably better preserved than with intensive sedation. The wounded arrive at hospitals ready for immediate operation without any additional anesthetic. Appropriate precautions against shock should be taken if a tourniquet has been in place for eighteen hours or longer. When any parts are potentially infected, refrigeration holds everything in abeyance. Bacteria cannot grow or invade. Suitable postoperative temperature reductions should facilitate conservative and reparative operations and aid in avoiding amputations and crippling. Allen concludes that the chief difficulty will perhaps consist in persuading surgeons that a refrigerated limb, no matter how cadaveric, actually retains vitality. The most revolutionary achievements of the method may be hoped for in military and emergency surgery. Refrigeration introduces the fundamentally new concept of anesthesia of protoplasm.

Anesthesiology, New York

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Certain Physiologic Principles Underlying Resuscitation and Oxygen Therapy. A. R. Behnke, Washington, D. C.—p. 245.
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Vinethene: Recent Laboratory and Clinical Evaluation. S. J. Martin and E. A. Rovenstine, New York.—p. 285.
Theory of Anesthesia Based on Protoplasmic Behavior. W. Seifriz, Philadelphia.—p. 300.
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Histopathologic Changes in Rats Following Administration of Pentothal Sodium and Sulfanilamide. P. H. Lorhan, Gretchen Guernsey and M. Harless, Kansas City, Kan.—p. 326.
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*Precautions in Treatment of Thyrotoxicosis. W. H. Cole, Chicago.—p. 752.
*Endocrine Studies of Patients After Subtotal Hypophysectomy. P. Starr and L. Davis, Chicago.—p. 778.
*Acute Cholecystitis with Perforation into Peritoneal Cavity. C. R. Edwards, W. H. Gerwig and W. L. Guyton, Baltimore.—p. 824.
End Results in Repair of Inguinal Hernia by Fascia to Fascia Rectus Sheath Closure. W. L. Estes Jr., Bethlehem, Pa.—p. 838.
Management of Bilateral Renal Stones: Point of View of the General Surgeon. J. G. Sherrill and D. P. Hall, Louisville, Ky.—p. 851.
Surgical Treatment of Arthritis. F. D. Dickson, Kansas City, Mo.—p. 869.

Treatment of Thyrotoxicosis.—Cole suggests that fixed rules of treatment do not apply in thyrotoxicosis because the toxicity can be definitely measured by clinical and laboratory methods and the treatment varied accordingly. Since the advent of iodine in the preoperative care of thyrotoxicosis few instances of postoperative crisis are observed. If a crisis develops an error has been made in the date or extent of operation. In spite of all precautions there will be a small mortality rate, perhaps as high as 0.02 or 0.03 per cent, because of unpreventable accidents. The incidence of natural death alone during several days of hospitalization will prevent the establishment of a mortality rate of zero, except by coincidence, in a large series of cases. Occasionally complications may develop which are in reality secondary to the operation but which appear unpreventable. The probability that the higher

mortality rates in the South over those in the North are related to the higher incidence of Negroes in the thyrotoxic patients is not clearcut. In the author's series of 478 thyroidectomies for toxic goiter, performed during the last four and a half years, there were no deaths among the 42 Negro patients. It is possible that the Northern Negro is better nourished than the Southern Negro. It would appear that longer preoperative therapy would be indicated and that weight gain must be greater than in the average patient. Of 6 patients dying following operation, 2 died because of crisis, 1 because of gas gangrene of the buttocks, 1 because of postoperative hemorrhage, 1 because of tetany and 1 because of acute hepatitis. All of these deaths were of white women. At least half of them were preventable, particularly the 2 patients in crisis and the 1 patient dying from postoperative hemorrhage. Neither of the 2 patients dying from crisis fulfilled the prerequisites as set forth by the author: gain in weight, basal metabolic rate below 50, a resting pulse of less than 110 and a response to iodine treatment. If these prerequisites cannot be met, operation should be postponed and a remission awaited or the patient submitted to removal of only one lobe. The 2 cases should be classified as errors in the choice of time of operation. The patient who died from hemorrhage into the neck could probably have been saved by more careful postoperative observation with opening of the wound and evacuation of the clot. The total operations were performed by twelve different surgeons. Hepatic insufficiency is a contributing cause of death in many instances. However, Foss and his associates were unable to find a direct relationship of the amount of hepatic damage to the severity of the crisis in patients dying of thyroid disease.

Endocrine Studies After Subtotal Hypophysectomy.—Starr and Davis determined the endocrine function of patients who have had subtotal hypophysectomies with the intention of giving substitution therapy to the patients who have had nonfunctioning tumors of the hypophysis and of ascertaining the necessity for further depressant therapy for those having hyperfunctioning pituitary adenomas. Eighteen of the 25 patients studied had hypopituitarism, the others hyperpituitarism. The 18 patients exhibited hypopituitarism before operation, occasionally with cerebral damage accompanying the visual disturbance. The hypopituitarism continued after the operation; the nervous disorder of some was improved but in others it was increased; the visual loss was usually arrested or relieved, but blindness developed in some patients a few years after operation. Of the 7 patients with hyperpituitarism, none have had postoperative hypopituitarism; 3 have persistent hyperpituitarism, 2 of these with manifest hyperthyroidism, diabetes and hypertension. Clinically all of this group presented acromegaly. In the 3 disabled patients acromegaly was severe before operation and in the 4 well adjusted patients the acromegaly was slight. In the hypopituitary group hypometabolism is the rule. The blood cholesterol is significantly raised in the 4 patients with the lowest rates (between —30 and —40 per cent) indicating thyroid deficiency; however, in only 6 of 11 at —20 per cent is it elevated; in the other 5 it is normal, indicating that their hypometabolism is not associated with relative hypothyroidism. Thyroid administration would be of value in 10 of the hypopituitary patients to judge by hypercholesterolemia. Adrenal insufficiency was indicated by abnormally high chloride concentrations in the urines of 5 of the hypopituitary patients and in 1 of the hyperpituitary group. The 2 patients with the highest tests (as high as those found in fully developed Addison's disease) are in excellent clinical condition carrying on normal lives. This suggests that in some way the hypopituitary state of these patients avoids the sodium depletion that leads to the crises which occur in Addison's disease. Consideration of the sugar tolerance curves shows greater tolerance to sugar in the hypopituitary group but the flatness is rarely pronounced and the curves usually are entirely normal. The hyperpituitary group have a higher curve; that is, lower tolerance to sugar. This was most pronounced in the 2 patients with active acromegaly. Five of the 7 patients have abnormally high sugar tolerance curves. The more hypopituitary patients had greater susceptibility to insulin and 3 of the 7 hyperpituitary patients were unaffected by the insulin tolerance test. However, 1 of them had a well defined insulin effect in combination with a high sugar tolerance curve. Sexual function and the condition of the sex organs indicated great deficiency in all but 3 of the hypopituitary patients. In the exceptions, normal gonadal development and function were maintained. In the hyperpituitary group, 2 were normal; in addition, 2 women had amenorrhea and hot flashes indicative of pituitary activity characteristic of the menopause, and 1 male had impotence and atrophy similar to that of the deficiency group. The authors state that their experience indicates that diagnosis of hyperpituitarism associated with nonfunctioning pituitary or embryonal tumors is frequently missed. The diagnosis would be made earlier if patients presenting signs of sexual deficiency were studied with this in mind. In women, amenorrhea and obesity are early results; in men, loss of libido and diminished beard growth occur in the incipient stage. Endocrine studies emphasize the loss of individual pituitary functions which may be replaced by the administration of the hormones of the glands normally maintained by pituitary activity; this is especially true of the thyroid. This is at —20 per cent. Increasing the rate above this will place the hypopituitary patient in relative hyperthyroidism.

Acute Perforating Cholecystitis.—Edwards and his associates collected 21 cases from two Baltimore hospitals of gallbladder perforations into the free peritoneal cavity complicating acute cholecystitis. Such perforations cause a diffuse biliary peritonitis which is highly toxic and against which the peritoneum has little resistance. The patients have been under the care of several surgeons. The authors therefore believe that their report is suggestive of the actual percentage of perforations into the peritoneal cavity which might generally be anticipated. During eleven years at the Church Home and Infirmary there were 32,921 admissions, 531 of which were for gallbladder disease and among these there were 96 acute cases with 8 perforations into the peritoneal cavity, or 8.33 per cent. During six years at the University Hospital there were 34,958 admissions, of which 593 were for cholecystitis and among these 98 were acute with 13, or 13.31 per cent, perforations into the peritoneal cavity. With a total percentage of 10.82 this serious complication cannot be regarded as rare. It is generally conceded that patients with chronic cholecystitis may have their operation deferred while being thoroughly studied and prepared, but this policy cannot be applied safely to the acute instances. This is clearly illustrated by the fact that operation was possible for only 6 of the 8 patients from the Church Home; the length of their illness prior to admission was short. The other patients were practically moribund on admission; they failed to respond to treatment and died from the overwhelming infection and toxemia. Twelve of the 13 patients of the University Hospital group were operated on. The remaining patient, ill less than twenty-four hours before admission, was not able to endure an operation. She failed to respond to treatment and died within eighteen hours of admission. There was 1 death among the Church Home group and 2 among the University Hospital group of patients. Bacteriologically, nothing new or unexpected has been observed among these 21 patients. The colon bacillus was recovered from the gallbladder of 6, Streptococcus faecalis from 1, Streptococcus nonhaemolyticus from 1 and Staphylococcus aureus from 1; no growth was recorded from 4 and no culture was made of the remaining 8. No attempts were made to find any pancreatic enzymes; while the regurgitation of pancreatic and duodenal juices into the gallbladder is possible under some circumstances, it is inconceivable, in view of the pathologic changes encountered in the biliary system of the patients considered. The leukocyte count averaged from 18,000 to 20,000. Other laboratory tests were of no value in determining the severity of the infection. Febrile reactions and pulse rates were variable. Roentgenograms played no part in arriving at a diagnosis. The history and physical examination were so suggestive of gallbladder disease that they have been depended on without roentgenograms. The exquisite tenderness on the slightest pressure over the gallbladder area indicates peritoneal irritation, and if present over the entire abdomen it suggests a rapidly spreading biliary peritonitis. If after the administration of dextrose and salt solution intravenously the patient

looks and feels better but shows little or no improvement on palpation, an immediate operation is indicated. In the present series there were ten cholecystectomies, seven cholecystostomies and one partial resection of the gallbladder.

Archives of Dermatology and Syphilology, Chicago

43:763-922 (May) 1941

Endocrine Glands and Their Relation to Dermatology. E. L. Sevringhaus, Madison, Wis.—p. 763.
Phagedaena Geometrica (Brocq): Inoculation Studies with Viable Bacteria Cultured from Lesions of Phagedaena Geometrica (Brocq), Chronic Burrowing Ulcer and Pyoderma Gangraenosum. S. S. Greenbaum, Philadelphia.—p. 775.
Erythema Nodosum of Face: Report of Case. S. M. Bluefarb and G. E. Morris, New York.—p. 802.
Solitary Gummatous Sporotrichosis of Two Years' Duration: Report of Case. P. V. Graham, Wheeling, W. Va.—p. 805.
Pseudoactinomycotic Epithelioma of Face. H. Charache, Brooklyn.—p. 809.
Sarcoma Arising in Organized Hematoma Resulting from Single Trauma: Report of Case. J. J. Eller and L. H. Kest, New York.—p. 813.
Herpes Simplex: Case of Unusually Extensive, Recurrent Type, Apparently Cured After Autoserotherapy. Carmen C. Thomas, Philadelphia.—p. 817.
Necrobiosis Lipoidica: Form of Granuloma Annulare? F. A. Ellis, Baltimore.—p. 822.
Acute and Subacute Disseminated Lupus Erythematosus: Treatment with Liver Extract. T. Cornbleet, Chicago.—p. 829.
Acute Disseminated Lupus Erythematosus: Precipitation by Roentgen Rays and Cure with Sulfanilamide. H. H. Hopkins, Baltimore.—p. 833.
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Trichophytin: I. Methods of Preparation with Special Reference to Specific Skin-Reactive Factor. S. M. Peck and A. Glick, New York.—p. 839.

Archives of Neurology and Psychiatry, Chicago

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Neuropathologic Changes Associated with Experimental Anaphylaxis in Monkey. G. A. Jervis, A. Ferraro, L. Kopeloff and N. Kopeloff, New York.—p. 733.
*Altered Concept of Therapy of Involutional Melancholia with Estrogen and Androgen. N. O. Rothermich, Beatrice Postle and L. M. Foltz, Columbus, Ohio.—p. 752.
Dilantin Sodium Poisoning: Report of Case with Dermatitis Exfoliativa, Pyrexia and Hepatic and Splenic Enlargement. H. Mandelbaum and L. J. Kane, Brooklyn.—p. 769.
Peripheral Nerves in Cases of Nutritional Deficiency. C. D. Aring, W. B. Bean, E. Roseman, M. Rosenbaum and T. D. Spies, Cincinnati.—p. 772.
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Pick's Disease: Clinicopathologic Study and Report of Case. G. B. Hassin and D. Levitin, Chicago.—p. 814.
Electroencephalogram of Children with Focal Convulsive Seizures. L. Casamajor, J. R. Smith, Kate Constable and C. W. P. Walter, New York.—p. 834.
Changes in Retinal Arteries Before Convulsions Induced by Electric Shock. E. C. Milch, New York.—p. 848.

Involutional Melancholia.—Rothermich and his colleagues used estrogen or androgen for the treatment of 24 women exhibiting depressive psychoses associated with or following the menopause. The 12 patients treated with theelin received 1 mg. three times a week until at least 20 mg. was given, and those given androgen received 35 mg. of testosterone three times a week for one month and then 25 mg. three times a week until a minimum of 800 mg. was injected. The total doses and duration of treatment were determined by the response. Fourteen patients presented the classic picture of involutional melancholia and 10 an atypical picture. The changes in the physiologic state (gain in weight and a tendency toward normal, dextrose tolerance, cholesterol and metabolic rate) of all patients were definite. The response in the vaginal smear and the excretion of gonadotropin in the urine of the patients who received theelin presented the usual "follicular" changes in the vaginal smear, while the smears of those treated with testosterone indicated conversion to or persistence in the atrophic state, depending on the previous condition. Approximately half of the patients had abnormally high excretions of gonadotropin prior to therapy. Following therapy this was reduced to within normal limits in all but 1. Regular cyclic menstruation reappeared in 6 of the patients showing psychiatric improvement. Five of these are still having monthly periods more than a year after treatment was discontinued. The other patient had eight regular periods; these were followed by typical menopausal symptoms. Psychiatrically 12 patients showed some benefit from the therapy. The criterion of improvement was the ability to return home and carry on fairly well in their own environment. Some of the patients designated as unimproved showed various degrees of decreased agitation and depression but were unable to return to their homes and hence are said to have shown no significant improvement. Only 5 of the 14 patients with classic melancholia were benefited. As spontaneous recovery is generally considered to be slightly higher than 25 per cent, the 35 per cent of results can hardly be considered therapeutically significant. In the other, or "atypical," group, 7 of the 10 patients showed clinical improvement or recovery. Follow-up studies for as long as eighteen months of these 7 patients bore out the consistency of the results in all but 2; 1 patient had been home for two months when she suffered a complete relapse and of the 12 patients who showed improvement 7 received testosterone. Of 7 in the atypical group who improved, 4 were treated with testosterone and 3 with theelin.

Archives of Ophthalmology, Chicago

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Results of Surgical Treatment of Paralysis of Superior Oblique and Superior Rectus Muscles. S. R. Gifford, Chicago.—p. 761.
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Biochemistry of Lens: XIII. Production of Lens Opacities by Injection of Hypertonic Solutions. J. G. Bellows and H. Chinn, Chicago.—p. 796.
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Dark Adaptometer Readings of Subjects on Diet Deficient in Vitamin A. W. J. Dann and M. E. Yarbrough, Durham, N. C.—p. 833.
Effects of Some Silver Salts on Eye: (Silver Nitrate, Silver Ammonium Nitrate, Silver Ammonium Sulfate, Silver Ammonium Lactate and Mixture of Silver Ammonium Nitrate and Silver Ammonium Sulfate). H. O. Calvery, H. D. Lightbody and B. Rones, Washington, D. C.—p. 839.
Sympathetic Ophthalmia Caused by Nonperforating Intraocular Sarcoma. M. H. Riwchun and E. DeCoursey, Buffalo.—p. 848.
Practical Applications of Dynamic Retinoscopy. J. I. Pascal, New York.—p. 859.
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Archives of Otolaryngology, Chicago

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Collapse of Nares. A. A. Cinelli, New York.—p. 683.
Osteomyelitis of Frontal Bone: Report of Three Classified Cases. J. B. Stevens, Los Angeles.—p. 694.
Nitrogen Monoxide and Oxygen for Anesthetization in Operations for Malignant Growths of Larynx. J. I. Kemler, Baltimore.—p. 707.
Concentration of Menthol in Smoke from Mentholated Cigarets: Study of Local and Systemic Effects. H. W. Haggard and L. A. Greenberg, New Haven, Conn.—p. 711.
Acute Streptococcic Laryngotracheobronchitis. E. S. Connell and B. C. Trowbridge, Kansas City, Mo.—p. 717.
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Acute Suppurative Otitis Media: Review of Cases Encountered During Five Year Period. E. A. Stuart, Montreal, Canada.—p. 734.
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Acute Laryngotracheobronchitis: Report of Case and Review of Literature. R. Kayser, Brooklyn.—p. 795.
Patency of Eustachian Tube in Relation to Profound Hearing Loss in Childhood. C. Y. Mao, Shanghai, China, and W. Hughson, Abington, Pa.—p. 824.
Paranasal Sinusitis in Relation to Systemic Disease, with Special Reference to Diagnostic Lavage. J. L. Goldman, New York.—p. 830.
Tuberculosis of Upper Respiratory Tract: Review of Literature of Past Two Years. G. B. Wood, Philadelphia.—p. 861.

Archives of Pathology, Chicago

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*Pinealoma. J. H. Globus, New York.—p. 533.
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Relation of Experimental Pulmonary Arterial Hypertension to Arteriosclerosis. H. T. Karsner, M. A. Simon and T. F. Fujiwara, Cleveland.—p. 585.
*Changes in Urinary Tract and Other Organs After Administration of Three Sulfanilamide Derivatives. W. Antopol, D. Lehr, J. Churg and H. Sprinz, Newark, N. J.—p. 592.
Brain Degeneration in Young Chicks Reared on Iron-Treated Vitamin E-Deficient Ration. F. B. Adamstone, Urbana, Ill.—p. 603.
Erythrophagocytosis in Chicks Reared on Vitamin E-Deficient Ration Supplemented with Halibut Liver Oil. F. B. Adamstone, Urbana, Ill.—p. 613.
Histologic Evidence Indicative of Natural Occurrence of Vitamin E Deficiency in Chick. F. B. Adamstone, Urbana, Ill.—p. 622.
Tattoos. G. J. Rukstinat, Chicago.—p. 640.

Pinealoma.—Globus cites 12 cases of pinealoma and stresses the microscopic character of the features of the tumor which link it to one or another histogenetic stage in the normally developing pineal body. The site of origin of the tumors was the quadrigeminal plate. A few of them appeared to be partly encapsulated, but the majority displayed an invasive character. Bilateral symmetrical hydrocephalus was always found. This is explained by the effect of the neoplasm on the underlying aqueduct of Sylvius and the resultant obstruction to the outflow of the cerebrospinal fluid. A microscopic pattern reduplicating one or another stage of the normal developing pineal body was established in every instance. In spite of the apparent cellular divergence, the structural similarity and their common pineal origin was established. It was possible to match the structure of any one of the tumors with one or another histogenetic phase of the normal pineal body and thus trace them to the common source, an embryonal rest of the pineal body. The clinical manifestations, especially the symptoms and signs of increased intracranial tension, are readily explained by the direct and indirect influence of the tumor on territorial divisions of the brain stem. The symptoms and signs include progressively intense headache, nausea, recurrent projectile vomiting, dizziness and papilledema. Diplopia, explained by the effect of the tumor on the oculomotor nuclei, occurs frequently. Argyll Robertson pupils are most frequently encountered. Skew deviation, often associated with involvement of the brachia conjunctiva, is also a fairly frequent observation. The explanation for disturbances of vegetative functions is found in the hydrocephalus caused by the effect of such a tumor on the aqueduct of Sylvius. The coincident dilatation of the third ventricle results in alterations in the hypothalamus, the part of the brain stem concerned with regulating vegetative functions. The coexistence of vegetative disorders accompanied by disturbances in the development of sex character suggests the probability that the normal evolution of sex character is but an expression of vegetative (visceral) organization of the organism. By shifting the control of the development of sex character from the pineal body to the hypothalamus, an explanation may be found for the relative infrequency of pubertas praecox in verified cases of pinealoma. The proximity of the tumor to the converging dentorubral fibers is in part responsible for the awkward use of the extremities, as unsteadiness, wide gait and other forms of ataxia. Pyramidal tract signs (paresis of the extremities, elevated deep reflexes and pathologic reflexes) are frequent. Extrapyramidal tract signs (tremor, loss of associated movements and decerebrate rigidity) are encountered.

Organic Changes After Sulfanilamide Therapy.—Antopol and his collaborators studied the macroscopic and microscopic organic changes in albino rats after single and after repeated intraperitoneal injections of the sodium salt of sulfapyridine, sulfathiazole and sulfamethylthiazole. Complete necropsies were made on more than 150 animals, special attention being given to the urinary tract. A high incidence of intrarenal precipitation and urolith formation, accompanied by severe damage to the kidneys and liver, was seen after the injection of sodium sulfamethylthiazole. The administration of large doses of sodium sulfathiazole was invariably followed by acute massive precipitation of the free drug in the urinary tract. This phenomenon is assumed to be due to its high rate of elimination and the lack of reabsorption from the renal tubules. The precipitation in the collecting tubules was noncrystalline. On repeated administration renal concrements could be produced with each compound, and they were due to the formation of the insoluble acetylated derivatives of the compounds. Calcifying nephrosis of varying degrees, generally of the distal convoluted tubules, sometimes also of the collecting tubules, usually accompanied the concretions. A single intravenous injection of any of the sodium salt acetylated derivatives produced severe, extensive calcifying nephrosis. Utmost care should be exercised when sulfamethylthiazole is used, as this drug is apt to cause severe renal and hepatic lesions, and sulfathiazole seems more apt to produce renal damage than sulfapyridine. This is probably because of the higher insolubility of its acetylated compound and possibly because of its acute precipitation of free sulfathiazole in the urinary tract.

Archives of Surgery, Chicago

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Carcinoma of Large Intestine: Review of 416 Autopsy Records. R. E. Buirge, New Hampton, Iowa.—p. 801.
Surgical Lesions of Pancreas: Review. W. Walters and W. H. Cleveland, Rochester, Minn.—p. 819.
Paralysis of Conjugate Lateral Movement of Eyes in Association with Cerebellar Abscess. P. C. Bucy, Chicago, and T. A. Weaver Jr., Cincinnati.—p. 839.
Instrumental Perforation of Rectosigmoid. H. E. Pearse, Rochester, N. Y.—p. 850.
Pneumatocele Occipitalis. B. Woodhall, Durham, N. C., and T. W. Baker, Charlotte, N. C.—p. 858.
Selection of Cases for Peritoneoscopy. C. A. Beling, Newark, N. J.—p. 872.
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Basal Cell Carcinoma in Youth: Report of Case. R. L. Sewell, Rochester, N. Y.—p. 909.
Tic Douloureux: Relation of "Trigger Zones" to Painful Seizures; Report of Case. O. R. Hyndman, Iowa City.—p. 913.
Differential Sensitivity of Sarcoma and Normal Tissues to Temporary Arrest of Circulation. P. Salzburg and H. Kabat, Minneapolis.—p. 917.
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Pathology of Dehydration Shock. H. A. Davis, New Orleans.—p. 939.
Nondestructive Tuberculous Polyarthritis versus Tuberculous Rheumatism (Poncet): Report of Case. D. H. Kling and M. A. Levine, Los Angeles.—p. 956.

California and Western Medicine, San Francisco

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Chronic Gallbladder Disease: Preparation of the "Bad Risk" Patient. H. G. Bell, San Francisco.—p. 269.
Sinus Infections: Their Relationship to Respiratory Disease. F. Arnold, Long Beach.—p. 270.
Primary Repair of Tendons: Study of End Results in 207 Cases. M. Debenham, San Francisco.—p. 273.

Canadian Medical Association Journal, Montreal

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Anesthesia in Patient with Pulmonary Tuberculosis. H. E. Pugsley and G. D. Richardson, Gravenhurst, Ont.—p. 473.
Clinical Study of Inferior Turbinate Cavernous Tissue: Its Divisions and Their Significance. H. H. Burnham, Toronto.—p. 477.
Osteitis Deformans (Paget's Disease). M. Siegel, Hamilton, Ont.—p. 482.
Use of Newer Drugs. W. H. Brown, Camp Borden, Ont.—p. 485.
Pneumonia in Infancy and Childhood. N. Silverthorne, A. Brown and W. J. Auger, Toronto.—p. 496.
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Endocrinology, Los Angeles

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Influence of Epinephrine and Adrenal Cortical Extract on Lactogenic Property of Prolactin. D. R. Climenko and E. W. McChesney, Rensselaer, N. Y.—p. 710.
Electrophoresis of Antihormone Serums. K. W. Thompson and J. L. Melnick, New Haven, Conn.—p. 723.
Increased Estrogenic Potency of Human Urine After Zinc Hydrochloric Acid Hydrolysis. O. W. Smith and G. Van S. Smith, Brookline, Mass.—p. 740.
Endocrine Factors Influencing Tumor Development: Effect of Gonadotropins and of Theelin on Marsh-Buffalo Adenocarcinoma and Lymphosarcoma. F. Bischoff, M. Louisa Long, J. J. Rupp and Georgena J. Clarke, Santa Barbara, Calif.—p. 769.
Effect of Hyperpyrexia on Spermatozoa Counts in Men. J. MacLeod and R. S. Hotchkiss, New York.—p. 780.
Bromine and Thyroid. E. J. Baumann, D. B. Sprinson and D. Marine, New York.—p. 793.
Nitrogen Metabolism in Hyperthyroidism. B. Sure, Z. W. Ford Jr., R. M. Theis and M. Goldfischer, Fayetteville, Ark.—p. 806.
Influence of Iodine Feeding on Normal Thyroid with Reference to Its Relative Potency in Stimulating Metabolism and Heart Rate. A. E. Meyer and Helen Danow, with technical assistance of Alice V. Hellegers, Brooklyn.—p. 816.
Effect of Steroid and Pituitary Hormones on Experimental Diabetes Mellitus of Ferrets. G. Dolin, S. Joseph and R. Gaunt, New York. —p. 840.

Journal of Clin. Endocrinology, Springfield, Ill.

1:375-460 (May) 1941. **Partial Index**

Therapy in Cushing's Syndrome: Cushing's Syndrome Interpreted as Hyperadrenocorticism Leading to Hypergluconeogenesis: Results of Treatment with Testosterone Propionate. F. Albright, W. Parson and Esther Bloomberg, Boston.—p. 375.
*Insulin Resistance: Critical Survey of Literature with Report of Case. W. P. Martin, Helen Eastman Martin, R. W. Lyster and S. Strouse, Los Angeles.—p. 387.
Id.: Association of Extreme Insulin Resistance with Allergy: Report of Case. J. F. Hart and C. A. Vicens, New York.—p. 399.
Hyperinsulinism: Asthma, Diabetes Mellitus and Hyperinsulinism. E. M. Abrahamson, Brooklyn.—p. 402.
Inhibition of Lactation: Percutaneous Use of Testosterone. A. J. Fleischer and J. I. Kushner, New York.—p. 407.
Stilbestrol: Use of Stilbestrol in Suppression of Lactation. S. D. Soule and A. R. Bortnick, St. Louis.—p. 409.
Id.: Treatment of Menopause with Stilbestrol. S. G. Taylor 3d and W. O. Thompson, Chicago.—p. 411.
Homosexuality: Criteria for Hormone Explantation of the Homosexual. A. C. Kinsey, Bloomington, Ind.—p. 424.
Hypopituitarism: Simmonds' Disease Associated with Pernicious Anemia, with Bioassay of Large Chromophobe Adenoma. M. A. Foster and J. C. McCarter, Madison, Wis.—p. 436.
Pituitary Pathology: Vacuolization of Basophil Cells of Pituitary Body (Pars Distalis) in Relation to Age, Menstruation and Thyroidism. A. D. Ecker, Syracuse, N. Y.—p. 442.
Acromegaly: Thyroid Gland in 166 Cases of Acromegaly. A. C. Davis, Rochester, Minn.—p. 445.
Dihydrotachysterol: Modern Treatment of Parathyroid Insufficiency. F. Holtz, Berlin, Germany.—p. 453.

Insulin Resistance.—Martin and his colleagues consider patients resistant to insulin when after forty-eight hours of observation 200 or more units of insulin fails to bring about an appreciable lowering of the blood sugar. Cases of insulin resistance of both known and unknown etiology are included in this definition. The known factors are acidosis, infection, sepsis, overactivity of the physiologic antagonists of the pancreas, pituitary, thyroid and adrenal, and hepatic disease such as hemochromatosis. The definition is arbitrarily made on the combined basis of time and the amount of insulin. The precipitating factor in a case reported by the authors was apparently hypersensitivity to protamine zinc insulin, which produced a generalized urticaria. Although these lesions cleared in three days following cessation of protamine zinc insulin and the administration of calcium gluconate, the expected response to crystalline insulin or to regular insulin was not forthcoming. The patient's history of the development of an itching erythematous lesion of the head and neck three years earlier suggested an allergic background, although the condition was not diagnosed as such. The early lesion was not caused by protamine zinc insulin. Infection is a frequent cause of insulin resistance, although the resistant phase is usually transient. Local peritonitis about the cecum observed at necropsy in their patient was not suspected during life, and the authors believe that it developed shortly before death. The incidental finding of a small hypernephroma further complicated the picture, although there is little likelihood that it had any bearing on the resistance. On the second day following admission to the hospital 995 units of insulin and on the next day 1,190 units was used. At this time the blood sugar dropped from 541 to 295 mg. per hundred cubic centimeters and the carbon dioxide combining power rose from 18 to 48 volumes per cent. The next day only 205 units of insulin was necessary to maintain the blood sugar between 221 and 294 mg., while the carbon dioxide combining power steadily rose to 60 volumes per cent. However, within forty-eight hours of observation 275 and 255 units of insulin on two successive days was insufficient, as the blood sugar rose slowly and the carbon dioxide combining power diminished. It is possible that, had the significance of the associated allergic state with insulin resistance been appreciated and had massive doses of insulin been continued during these two critical days, death might have been averted. In reviewing cases reported as examples of insulin resistance, the authors had difficulty in selecting those which fell into their classification and definition. Immediately after the discovery of insulin, many examples of presumed insulin resistance were published which in fact were only temporary changes in insulin need. Only those examples of insulin resistance which lasted forty-eight hours or longer and required 200 or more units of insulin daily are tabulated in detail; there are 5 cases due to disturbances of the endocrine glands, 5 due to infection (pyelitis, sepsis or tuberculosis), 5 due to hepatic disorders, 8 due to cutaneous and allergic disorders (urticaria, eosinophilia and bronchial asthma) and 2 unexplained cases. The first step in the treatment of insulin resistance is to determine the etiology and to eliminate it if possible. Insulin sensitivity should be tested for and the type and brand and route of administration should be changed if necessary. Crystalline insulin is least likely to produce allergy. Evidence indicates that there is not necessarily any upper limit to the number of units of insulin which may be given. General therapeutic measures should be directed against all the possible contributory factors. Other empiric measures worthy of trial include endocrine therapy (estrogenic preparations, solution of parathyroid), intravenous phosphate solutions, change in type of carbohydrate in the diet, vitamin B, pituitary irradiation and desensitization.

Journal of Clinical Investigation, New York

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Further Observations on Skin Reactions to Antigens from Heterologous Cestodes in Echinococcus Disease. J. T. Culbertson and H. M. Rose, New York.—p. 249.
Calcium and Phosphorus Metabolism in Osteomalacia: XI. Pathogenic Role of Pregnancy and Relative Importance of Calcium and Vitamin D Supply. S. H. Liu, H. I. Chu, H. C. Hsu, H. C. Chao and S. H. Cheu, Peiping, China.—p. 255.
*Observations on Effect of Streptococcic Upper Respiratory Infections on Rheumatic Children: Three Year Study. Ann G. Kuttner and Elma Krumwiede, Irvington-on-Hudson, N. Y.—p. 273.
*Epidemic of Influenza B Occurring in Group of Rheumatic Children Concurrent with Outbreak of Streptococcic Pharyngitis: Clinical and Epidemiologic Observations. Gertrude Reyersbach, T. F. Lenert and Ann G. Kuttner, Irvington-on-Hudson, N. Y.—p. 289.
Studies of Calcium and Phosphorus Metabolism: XVI. Influence of Pituitary Gland. W. Bauer and J. C. Aub, Boston.—p. 295.
Acid-Base Balance, Renal Function and Gastric Secretion During Hypochloremia in Dog. J. B. Kirsner and Kathryn Knowlton, Chicago.—p. 303.
Clinical Studies on Pyridoxine (Vitamin B_6)). J. Flexner and M. R. Chassin, New York.—p. 313.
Demonstration That the Cell Plasma Ratio of Blood Contained in Minute Vessels Is Lower Than That of Venous Blood. R. V. Ebert and E. A. Stead Jr., Boston.—p. 317.
Clearance of Bilirubin from Plasma: Measure of Excreting Power of Liver. A. A. Weech, Dorothea Vann and Rose A. Grillo, New York. —p. 323.

Streptococcic Respiratory Infections and Rheumatic Fever.—Kuttner and Krumwiede studied over a period of three years the association between streptococcic infections of the upper part of the respiratory tract and rheumatic fever in 108 children who had had one or more attacks of polyarthritis or carditis without severe cardiac damage. The subjects lived and went to school in the same building at the Irvington House, a sanatorium for rheumatic children. They had no contact with other children, and each child was permitted only two adult visitors every six weeks. The group varied in age from 6 to 15 years. Rectal temperatures and pulse rates were taken

three times daily. Leukocyte counts, hemoglobin estimations and erythrocyte sedimentation rates were done every three or four weeks. Children with symptoms of infection of the upper part of the respiratory tract were put to bed in isolated cubicles or in separate rooms. Leukocyte counts were taken on the first or second day of illness. Three outbreaks of streptococcic infection occurred during three successive winters. Each epidemic was associated with group A beta hemolytic streptococci of a single but a different prevalent type. The incidence of rheumatic recurrences following the three waves of streptococcic pharyngitis varied. In the first, following a latent period, half the children showed signs of rheumatic activity, in the second all the children escaped rheumatic sequelae and in the third recurrence developed in a small proportion. A comparison of the streptococci associated with the recurrences and the "noneffective" strain failed to show any significant differences. Following infection with the two "effective" strains of streptococci, rheumatic recurrences developed sporadically over months. It is therefore assumed that these organisms carried the hypothetic rheumatic factor throughout the epidemics. As in many children who had streptococcic pharyngitis demonstrable signs of rheumatic activity did not develop, it is suggested that these individuals may have been in a refractory state. Thirty-one children who contracted the "effective" streptococcus type 27 pharyngitis within five years following their first attack of polyarthritis or carditis escaped cardiac involvement. During 1937-1938 the probable source of the epidemic strain was a patient who was a streptococcus carrier; during 1938-1939 and 1939-1940 the probable sources were 2 children who had acute infections of the upper part of the respiratory tract as the result of outside contacts. During all three years a fairly large proportion of the children were carriers of group A beta hemolytic streptococci of various types, which in most instances did not spread or cause pharyngitis. Some of these carrier strains had capsules and formed mucoid colonies. It is the authors' impression that instances of pharyngeal infection due to types of streptococci not previously present in the community are the most likely sources of epidemic strains. Therefore the exclusion of rheumatic children from sanatoriums or convalescent homes because they are carriers of small or moderate numbers of group A beta hemolytic streptococci does not seem warranted. Many children who have had streptococcic pharyngitis continue to harbor streptococci for months after recovery. There is no effective way of clearing up streptococcus carriers, and it is not feasible to isolate children for months at a time. The role of group A beta hemolytic streptococci in regard to rheumatic fever is analogous to that which prevailed in regard to scarlet fever before the discovery of erythrogenic toxin and the Dick test. Yearly fluctuations in the resistance of rheumatic individuals may be more important in precipitating rheumatic recurrences than qualitative or quantitative differences between strains of streptococci. The study of the relationship of streptococci to the etiology of rheumatic fever should be continued, with the thought in mind that streptococci may be indicators which accompany the invasion or reactivation of a hypothetic rheumatic agent. The entrance or increased activity of this agent may enhance the infectivity of streptococci. If this hypothesis is true, the failure of rheumatic sequelae to develop in some children following pharyngitis due to "effective" strain of streptococci might be explained on the basis that reinfection with exogenous rheumatic "virus" or reactivation of endogenous rheumatic "virus" had not taken place at that particular time.

Influenza B and Streptococcic Pharyngitis in Rheumatic Children.—According to Reyersbach and her co-workers, in February 1940 a third type of infection of the upper part of the respiratory tract, an epidemic influenza, was observed for the first time at Irvington House. The influenza developed in rapid succession in 50 of the rheumatic children housed there. The outbreak is of special interest because a new virus serologically distinct from influenza A was isolated. The immunologic studies of Francis showed that the same or a closely related etiologic agent was also responsible for other epidemics occurring in widely separated parts of the United States. He designated the virus influenza B. The symptoms caused by influenza B closely resembled those associated with influenza A infection. The disease was mild, with constitutional rather than catarrhal symptoms predominating. Leukocyte counts of the 50 influenza B patients showed a relative leukopenia. Pharyngitis due to type 27 group A beta hemolytic streptococci was prevalent in the community before the influenza B epidemic. No evidence was obtained to suggest that influenza B facilitated the spread of group A beta hemolytic streptococci. The explosive character of the influenza B outbreak indicated that all susceptible individuals contracted the infection in a relatively short time. Susceptibility to the streptococcus type 27 pharyngitis was less severe; new cases developed over a period of six months. The susceptibility of the same child varied from time to time. In spite of intimate exposure to the streptococcic infection, pharyngitis failed to develop in some children and did so only several weeks later. The most striking difference was the absence of signs and symptoms referable to the upper respiratory tract in most influenza B infections. In the streptococcic infections nearly all the patients complained of "sore throat," and definite inflammation of the pharynx was usually apparent. The most valuable laboratory finding in establishing the diagnosis of influenza B was the leukocyte count. By this means it was usually possible to differentiate cases of the virus infection from streptococcus type 27 pharyngitis on the first day of illness. A relative leukopenia was found in all patients with influenza B and a definite leukocytosis in most patients with the streptococcic infection. Following a latent period rheumatic recurrences developed in 8 of the 39 patients who had the streptococcus type 27 pharyngitis, whereas no instance of a rheumatic exacerbation followed the influenza B infection.

Journal Industrial Hygiene & Toxicology, Baltimore

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X-Ray Diffraction: Important Tool in Pneumoconiosis Research and New Method of Tissue Analysis. L. H. Berkelhamer, New York.—p. 163.

*Silicosis in Soft Coal Miners. B. G. Clarke and C. E. Moffet, Cambridge, Mass.—p. 176.

Fundamental Factors in Design of Lateral Exhaust Hoods for Industrial Tanks. L. Silverman, Boston.—p. 187.

Automatic Carbon Disulfide Recorder. B. E. White and W. R. Calvert, Lewistown, Pa.—p. 196.

Chemical and Physiologic Investigation of Electric Arc Welding: III. Coated Welding Rods. C. P. McCord, G. C. Harrold and S. F. Meek, Detroit.—p. 200.

Silicosis in Soft Coal Miners.—Clarke and Moffet present results of a roentgen study of chests and the occupational histories of 774 miners of bituminous coal. The subjects had had at least one year of experience in bituminous coal mining; 43, or 5.6 per cent, of them were retired or deceased employees or rejected applicants. Among the 774 workers there were 8 instances of nodulation, in 4 of which there was roentgen evidence of healed or active tuberculosis. Five of the men contracted silicosis working as underground coal loaders for from twenty-three to thirty-six years, 1 of the men had been an undercutting machine operator for sixteen years, 1 had been a rock driller for eleven years and 1, a Scotsman, may have acquired his condition abroad. Roentgen evidence of healed and active adult type tuberculosis appeared in 7.4 per cent of the miners, which is comparable with the figure of 6.5 per cent for a control group of steel plant workers. When the coal miners are grouped by duration of exposure, the incidence of adult type tuberculosis tends to increase with increased duration of employment; when grouped by age a similar higher incidence of tuberculosis appears among the older workers. The trend is probably not peculiar to coal miners, as when the control group of steel plant workers are grouped by age there is an increase on roentgen evidence of healed and active tuberculosis among the older men. In studying the incidence of silicosis among workers performing different occupations the authors find that, after twenty years of experience as bituminous coal loaders, silicotic nodulation may develop in them. In undercutting machine operators, who work under extremely dusty conditions, presilicotic pulmonary changes are apt to develop. Of these workers 67 per cent show peritruncal exaggeration after twenty years of exposure and 16.2 per cent of machinemen and drillers show peritruncal exaggeration as compared with 2.1 per cent among the 774 bituminous coal workers examined and 1 per cent among the steel plant workers studied.

Journal-Lancet, Minneapolis

61:143-202 (May) 1941

Child Psychiatry and Pediatrics. R. A. Jensen, Minneapolis.—p. 143.
Public Health Aspects of Premature Infant Care in Minnesota. V. O. Wilson and A. J. Chesley, Minneapolis.—p. 147.
Erythroblastosis Foetalis. R. V. Platou, Minneapolis.—p. 151.
Use of Fluids in Pediatrics. J. A. Anderson and M. R. Ziegler, Minneapolis.—p. 155.
Pediatrician and Orthodontist. W. Hyde, Minneapolis.—p. 161.
Congenital Diaphragmatic Hernia. O. S. Wyatt, Minneapolis.—p. 164.
Hemangiomas: Classification and Treatment. L. H. Winer, Minneapolis.—p. 168.
Evaluation of Nutritional Status of Children. Arild E. Hansen, Minneapolis.—p. 172.
Clinical Evaluation of Beta Lactose as Prelacteal Feeding. A. J. Moss, E. L. Strem and A. V. Stoesser, Minneapolis.—p. 175.
*Dilantin Sodium Therapy in Epileptiform Seizures of Children. Elizabeth C. Lowry, Minneapolis.—p. 178.
Easing Convalescence. E. K. Clarke, Minneapolis.—p. 181.
Essential Hypertension. T. D. Allen, Evanston, Ill.—p. 183.
Role of the General Practitioner in Detecting Tuberculosis. C. Northrop, San Haven, N. D.—p. 187.
X-Ray Therapy in Infections and Tumors. R. G. Allison, Minneapolis.—p. 190.

Phenytoin Sodium Therapy in Epileptiform Seizures.—Lowy used phenytoin sodium in the treatment of epileptiform seizures of 34 children from 5 months to 16 years of age. The children were placed on a water restriction diet (900 cc. a day). The dosage of phenytoin ranged from 0.2 to 0.4 Gm. daily, depending on the age and the tolerance of the child. Twenty-four had grand mal attacks, 2 had petit mal and 8 had seizures of both types. Two thirds of the children were treated for one year or more and one fifth for two years or more. The following results were obtained: In 3 there was a complete cessation of seizures, 19 were improved (only 5 moderately) and 12 were not benefited. In many the attacks became milder. The 65 per cent of favorable results are comparable to experiences of most workers, but some have reported a higher percentage of complete remissions. In all but 1 (whose seizures ceased) of the 23 children who received phenytoin sodium continuously for a year or more the benefit was maintained throughout the period of observation without any increase in dosage, indicating that in general children do not acquire a tolerance for the drug. Most of the patients felt no ill effect from the medication. Patients with the most frequent attacks were most benefited. Phenobarbital and phenytoin sodium was given to patients whose response to the latter medication was unsatisfactory, and enough of these children improved to suggest that the combination was worth trying when other methods failed.

Journal of Neurophysiology, Springfield, Ill.

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Multiple Motor Innervation of Frog's Sartorius Muscle. B. Katz and S. W. Kuffler, Sydney, Australia.—p. 209.
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Experimental Study of Gastric Activity Released from Cortical Control. F. H. Hesser, O. R. Langworthy and L. C. Kolb, Baltimore.—p. 274.

Journal of Pharmacology & Exper. Therap., Baltimore

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Comparison of Ephedrine and Eserine. J. D. P. Graham and M. R. Gurd, Oxford, England.—p. 48.
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*Method for Determining Loss of Pain Sensation. F. E. D'Amour and D. L. Smith, Denver.—p. 74.
Action of Prostigmine on Circulatory System. R. Mendez and A. Ravin, Boston.—p. 80.
Action of Pitocin and Adrenalin on Different Segments of Rabbit Uterus. D. D. Bonnycastle and J. K. W. Ferguson, Toronto, Canada.—p. 90.
Comparative Effects of Sulfonamide Compounds as to Anemia and Cyanosis. A. P. Richardson, San Francisco.—p. 99.
Relationship Between In Vitro and In Vivo Activity of Sulfonamide Compounds. H. J. White, A. C. Bratton, J. T. Litchfield Jr. and E. K. Marshall Jr., Baltimore.—p. 112.

Determining Loss of Pain Sensation.—D'Amour and Smith determined the analgesic properties of cobra venom in doses of 4, 8 and 16 mouse units per kilogram of body weight, sodium amytal in doses of 25 and 50 mg., tarantula venom in doses of 10 milkings per rat, and black widow spider venom in doses of ⅛, ¼ and ½ lethal doses. Five opiates, dilaudid, morphine sulfate, codeine sulfate, diacetylmorphine and pantopon, were assayed at either three or four dosage levels, 12 rats being used for each dose level. By complete analgesia is meant the complete loss of reaction to pain: the animal makes no movement of the tail even though it is being burned to a crisp; however, a white blistering appearance is sufficient. The method used was to focus the rays from a Mazda 1184, from 6 to 8 volt bulb, with reflector, on the tip of the rat's tail, which was placed in a grooved board some 6 inches below. The setup includes a voltage regulator, transformer and rheostat; a stopwatch is operated by the same switch that makes and breaks the current. The operator places the rat's tail in the groove, switches on the light and stopwatch and waits for the response, which is a sudden, typical twitch of the tail when the animal feels the pain. After a few trials a light intensity which produced a reaction in about five seconds was found to be most convenient. The authors' assay of the opiates gave results in agreement with their accepted clinical value. A survey of doses recommended in a number of treatises indicates that dilaudid and diacetylmorphine are considered to be approximately four times as active as morphine, and codeine and pantopon about half as active as morphine. The results of the study approximated this ratio of effectiveness. The authors are unable to explain the discrepancy between their observations and those of Macht concerning cobra venom. On a dosage of 0.5 mouse unit (using 7 rats) he found an increase in the pain threshold, but in no case did the increase exceed the maximal stimulus (809 volts) found necessary at times in control rats. Only 2 rats were used on each of the higher doses, and the 2 on 2 mouse units gave inconsistent results in that the pain threshold in 1 was increased significantly (from 185 to 1,080 volts) but in the other only from 185 to 445 volts. The weight of the rats was not mentioned. In their study (the rats weighed approximately 250 Gm.) the authors noticed no effect on the reaction time. A dose of 16 mouse units per kilogram of body weight is approximately one half of the lethal dose. Although they make no claim that the method is capable of determining the analgesic power of drugs when deep seated, continuous pain is involved, nevertheless a method so simple and rapid should be of value in experimentally verifying many statements found in books on pharmacology the evidence for which rests usually on uncontrolled clinical impressions. Such questions as the influence on dosage of the route of administration and duration of analgesia, the analgesic properties of antipyretics, barbiturates and other drugs, the potentiating effects of one drug on another and the testing for analgesic properties of new drugs could be determined. The authors are engaged on certain of these studies.

Missouri State Medical Assn. Journal, St. Louis

38:143-184 (May) 1941

Chronic Cervicitis. G. F. Pendleton, Kansas City.—p. 143.
The Vagohypotonic Individual: Preliminary Report. D. G. Stine, Columbia.—p. 147.
Irritable Colon. J. M. Rumsey, Kansas City.—p. 152.
Use of Androgenic Hormone in Gynecology. S. Weber, St. Louis.—p. 155.
Pernio (Chilblains). C. L. Schaefer and C. E. Sanders, Kansas City.—p. 159.
Acute Anterior Poliomyelitis: Review. G. R. Peters and M. L. Peters, Cameron.—p. 160.

38:185-220 (June) 1941

Ideals of Medical Practice. C. E. Burford, St. Louis.—p. 185.
We Live to Serve and Not Serve to Live. R. B. Denny, Creve Coeur.—p. 187.
Practical Points in Meeting the Poor Surgical and Anesthetic Risks. R. R. Coffey, Kansas City.—p. 188.
*Treatment of Burns. W. R. Hewitt, St. Louis.—p. 191.
Improvement in Action of Procaine Salts in Caudal Anesthesia. M. M. Marks, Kansas City.—p. 196.
Infections of Urinary Tract: Treatment in General Practice. R. O. Pearman, St. Joseph.—p. 197.
Differentiation of Toxic Goiter from States Simulating Hyperthyroidism. R. W. Bartlett, St. Louis.—p. 200.

Treatment of Burns.—Hewitt discusses second degree burns which involve from 20 to 60 per cent of the surface of the body. Since 1935 he has followed the Davidson-Bettman method of treating burns with silver nitrate and tannic acid. On the face and hands a 2 per cent gentian violet is more

desirable, since it produces a thinner and more supple tan which, when it loosens about the eighth day, leaves a healed area. A triple dye may be used instead, but no method is completely satisfactory. The tannic acid and silver nitrate gives an eschar which leaves a viselike fixation of the eyelids which is uncomfortable and may lead to corneal ulceration. Greases of all sorts should be abandoned. In third degree burns coagulation should be avoided, and débridement and local dressing with petrolatum should be employed. As soon as the patient is in a bed tent and proper sedation and cleansing under anesthesia followed by swabbing with tannic acid and spraying with silver nitrate have been carried out, 1,000 cc. of plasma is administered to an adult and from 150 to 250 cc. to a child. Whole blood should be used to correct anemia and to combat infection. The danger of heat stroke exists when the outside temperature and humidity are high. Dusting with zinc stearate as the eschar rolls up is of value, but the danger of an allergic reaction exists. It is important to get the patient out of bed as soon as possible to prevent the development of a neurosis and to assist healing. Amphetamine sulfate is valuable in improving the patient's morale. Second degree burns of children become healed within twenty-one days if treated vigorously, and those of adults in from six to eight weeks. Some form of adrenal cortex should be given at once to prevent exhaustion or depletion of the reserve. Its value is not comparable to the use of plasma. Since protein enters into the chemical makeup of many hormones and enzymes, a minimum of 100 Gm. of meat daily may be of value, since it provides amino acids; two or three eggs may be added to the daily diet.

Nebraska State Medical Journal, Lincoln

26:119-158 (April) 1941

Sterility: The Internist's Examination of a Sterile Couple. J. C. Sharpe, Omaha.—p. 119.
Id.: The Urologist's Role. C. A. Owens, Omaha.—p. 121.
Id.: Physiology of Reproduction and Investigation of Sterility in the Female. W. E. Brown, Ann Arbor, Mich.—p. 123.
Prevention of Ivy Poisoning. W. H. Kerr, R. C. Danley, Hamburg, Iowa; L. A. Gaukel, P. L. Wolpert, Onawa, Iowa; L. S. Pucilek, Plattsmouth, and E. Cline, Auburn.—p. 129.
Hydranencephalus with Cerebellar Hemidysgenesis. J. Minckler, T. McCurdy and J. C. Iwersen, Omaha.—p. 131.
Curare in Treatment of Tetanus: Case Report. S. E. Isacson and S. A. Swenson Jr., Omaha.—p. 136.
Ideal Vaccination Technic. H. M. Page, Portland, Ore.—p. 138.
Smallpox in Nebraska. R. H. Loder, Lincoln.—p. 139.

26:159-198 (May) 1941

*Differential Diagnosis of Rheumatic Fever: Study of Diagnosis Made by Referring Physician in 167 Cases. A. E. Hansen, Minneapolis.—p. 159.
Tularemia. A. S. Rubnitz and A. M. Harris, Omaha.—p. 164.
Poliomyelitis: Case Report. E. V. Wiedman, Lincoln.—p. 170.
Id.: Physical Findings and Treatment. R. Stein, Lincoln.—p. 171.
Orthopedic Considerations in Poliomyelitis. C. F. Ferciot, Lincoln.—p. 173.
Fibroma of Transverse Colon: Report of One Case. E. A. Watson and D. P. Watson, Grand Island.—p. 175.
Progress in Prematurity Care. R. H. Loder, Lincoln.—p. 177.
Mantoux Test versus Vollmer Patch Test. J. D. LeMar, Omaha.—p. 180.
Scurvy. J. P. Tollman and R. L. Spradling, Omaha.—p. 184.

Differential Diagnosis of Rheumatic Fever.—Hansen reviews the diagnoses made by referring physicians on 167 children seen at the University of Minnesota Hospital from 1931 to 1940. In 28 instances the diagnosis of rheumatic fever was made. The condition most accurately and frequently diagnosed was chorea, this being present in 42 of the 167 cases. The diagnosis of rheumatic arthritis was made on 4 patients, while 3 patients were sent in because of joint stiffness and 2 because of joint pains. There were 23 referred with the diagnosis of rheumatic heart disease, while an additional 26 were sent in with such diagnoses as murmur, heart disease, heart infection, endocarditis, leakage of the heart, mitral heart disease and decompensation. Two instances were referred with a diagnosis of congenital heart disease. No diagnosis was given in 10. Of 27 with miscellaneous diagnoses 11 had abdominal pain, in 7 the diagnosis was appendicitis and in others it was poliomyelitis, osteomyelitis and septicemia. These data confirm the statements made in many pediatric textbooks that appendicitis, poliomyelitis, osteomyelitis, septicemia and certain cutaneous eruptions as well as various respiratory infections are frequently confused with rheumatic fever. In about one fourth of the patients the referring physician found it difficult to recognize the disease. On the other hand, the major symptoms were recognized as important in a high percentage of the patients, although carelessness was often exhibited in the use of the exact nomenclature. The highest degree of accuracy in the diagnosis of rheumatic fever is possible when one is thoroughly familiar with its varied manifestations.

New England Journal of Medicine, Boston

224:755-792 (May 1) 1941

Reduction of Pain and Other Undesirable Reactions Due to Pneumoencephalography. T. J. C. von Storch and H. H. Karr, Boston.—p. 755.
Estimation of Operative Risk in Patients with Cancer. A. S. Johnson, Springfield, Mass., and H. L. Lombard, Boston.—p. 759.
Prothrombin Level in Early Infancy: Its Relation to Hemorrhage and Other Neonatal Disturbances. G. Edsall, Boston.—p. 762.
Neurosurgery. D. Munro, Boston.—p. 766.

224:793-836 (May 8) 1941

Precancerous Dermatoses. O. S. Ormsby, Chicago.—p. 793.
*Acute Typhoid Cholecystitis and Cholelithiasis Occurring Forty-Three Years After Typhoid Fever: Report of Case. T. W. Botsford, Boston.—p. 799.
Clinical and Laboratory Observations on Hemoglobinuria Occurring During Sulfanilamide Therapy. D. R. Gilligan and I. Kapnick, Boston.—p. 801.
Bacteriology: Significance of Bacteriologic and Immunologic Procedures in Diagnosis and Treatment of Infections. C. A. Janeway, Boston.—p. 813.

Cholecystitis and Cholelithiasis Forty-Three Years After Typhoid.—Botsford cites an instance of acute suppurative cholecystitis due to Eberthella typhi forty-three years after the original attack of typhoid. The patient had her initial attack of cholecystitis a few weeks subsequent to recovery from the typhoid. Four attacks of cholecystitis followed at irregular intervals, but it was forty-three years after the typhoid that she was subjected to operation. The last attack was the most severe and was a true suppurative cholecystitis with perforation of the gallbladder and formation of an extravesical abscess. The virulence of the infective agent was demonstrated by the stormy clinical course. The high virulence of E. typhi was well demonstrated after forty-three years by the recovery of the organisms in pure culture from the bile, from the pus in the extravesical abscess and from the center of a gallstone. The patient, a mother of a large family, did all the cooking and yet she caused no known instance of typhoid. She must have been discharging typhoid organisms in her feces for years, if only intermittently. No stool cultures were made preoperatively, but of ten after the cholecystostomy tube was removed only two were positive for E. typhi. These positive cultures were the last of the series and were taken fourteen and thirty days respectively after the bile ceased draining through the tube. Because the patient was a poor operative risk, the gallbladder was not removed. Although drainage and removal of the stone still make her a typhoid carrier, the gallbladder is now free of a porous foreign body that contained E. typhi, and in time the viscus may become sterile. Under the circumstances it was probably wiser to have a living typhoid carrier than an operative fatality after a cholecystectomy.

New York State Journal of Medicine, New York

41:1123-1218 (June 1) 1941

Medical Problems in National Defense: From Point of View of the Army Medical Officer. C. M. Walson, Governors Island.—p. 1147.
Id.: Community Health in Areas Adjacent to Military Posts and in Defense Industries. A. E. Russell, Governors Island.—p. 1155.
Id.: From Point of View of the State Health Department. V. A. Van Volkenburgh, Albany.—p. 1158.
Id.: The Part of the Civilian Physician in the Defense Program. J. D. Naples, Buffalo.—p. 1163.
Subnormal Vision and Occupational Aptitude. A. C. Snell, Rochester.—p. 1165.
Practice of Radiology. H. K. Taylor, New York.—p. 1172.
Contrast Cineroentgenography of Circulatory Organs. W. H. Stewart, C. W. Breimer and H. C. Maier, New York.—p. 1174.
New Angle on Trigeminal Neuralgia: Study of 245 Cases with Observations on Seasonal Occurrence and Surgical Technic. H. W. Williams, Rochester.—p. 1177.
Amebic Dysentery as Complication in Diagnosis of Carcinoma of Rectum. A. A. Landsman, New York.—p. 1181.
Gallbladder Disease: Consideration of Mortality. C. G. Heyd, New York.—p. 1183.

North Carolina Medical Journal, Winston-Salem

2:165-216 (April) 1941

Etiology and Pathology of Cholecystic Disease. E. J. Wannamaker, Charlotte.—p. 165.
Signs and Symptoms of Cholecystic Disease. S. F. Le Bauer, Greensboro.—p. 166.
Roentgenologic Consideration of Cholecystic Disease. W. T. Rainey, Fayetteville.—p. 168.
Evaluation of Laboratory Procedures in Cholecystic Disease. E. B. Craven Jr., Lexington.—p. 170.
Diagnosis of Gallbladder Disease (Correlation of History, Physical Examination and X-Ray Evidence). W. M. Johnson, Winston-Salem.—p. 173.
Differential Diagnosis of Cholecystitis. W. R. Johnson, Asheville.—p. 175.
Management of Cholecystic Disease. J. M. Ruffin, Durham.—p. 177.
The Psychoneuroses. F. R. Taylor, High Point.—p. 178.
Primary Peritonitis. C. Bunch, Charlotte.—p. 184.
Prenatal Syphilis. J. M. Arena and D. E. Plummer, Durham.—p. 188.
History of Urology in North Carolina. J. S. Rhodes, Raleigh.—p. 191.
The Veterans Administration. B. A. Cockrell, Fayetteville.—p. 196.

Southern Surgeon, Atlanta, Ga.

10:301-378 (May) 1941

*Cod Liver Oil Therapy of Wounds and Burns. P. C. Hardin, Monroe, N. C.—p. 301.
Hormone Therapy of Fibromyomas of Uterus. R. B. Greenblatt and E. A. Wilcox, Augusta, Ga.—p. 339.
Diagnosis and Treatment of Ectopic Pregnancy. F. H. Falls, Chicago.—p. 347.
Treatment of Acute Fractures of Neck of Femur. H. B. Boyd, Memphis, Tenn.—p. 364.

Cod Liver Oil for Wounds and Burns.—Hardin reviews the literature on the use of cod liver oil as a dressing for wounds and burns and states that among its advantages as a dressing are the following: The oil is sterile and bactericidal, it is stimulating to granulation and epithelization, it accelerates liquefaction of dead tissue, it produces a beneficial local and systemic response and, as it also acts as a protective layer between the lesion and the dressing, each change of dressing is painless and as the gauze does not adhere to the wound there is no loss of the much needed blood from granulations. The author found cod liver oil therapy especially applicable to extensive crushing or destructive injuries, compound fractures, gunshot wounds, open amputation stumps, abscess cavities, large infected wounds, major primary burns and extensive ulcerations from burns or other causes: to sum up, for any injury with loss of tissue in which immediate surgical closure is not feasible. During the last five years he has used the oil as a dressing for 346 wounds and burns. During the first four years he used a home-made ointment composed of from 50 to 80 per cent of U. S. P. or high potency cod liver oil and petrolatum. During the last year he tried out six commercially manufactured cod liver oil ointments and he was not able to distinguish between their therapeutic activity. All were effective and all appeared definitely superior to home-made ointments. Each has a pleasing odor, a genuine advantage over the fish odor of home-made ointments. The commercial ointments keep indefinitely at room temperature and do not become rancid as does the home-made ointment. Case reports of the several types of lesions treated are reported, and it is pointed out that cod liver oil will not harm the most delicate tissues. It may be applied to the naked brain, the cornea, the exposed intestine and other tissues without fear of irritation or infection. The author reports the first cure with cod liver oil of a chronic undermining burrowing ulcer and 2 cases of complete rupture of an infected abdominal wound in which the oil was applied to the intestine. Cod liver oil is not offered as a panacea for all the evils of wound healing. Granulations often require trimming and the application of silver nitrate. At times a change from the oil to oxyquinoline scarlet R or bismuth violet ointment may be temporarily beneficial. Hot wet saline or boric acid compresses may be useful. The patient should always have the benefit of early skin grafting when necessary. General disease must be recognized and adequately treated. Hypoproteinemia must be prevented, the diet must be adequate and sufficient ascorbic acid intake is essential, while anemia must be prevented or the condition corrected.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

49:197-258 (April) 1941

Appendicitis. C. E. Black, Jacksonville, Ill.—p. 197.
Surgery of Biliary Tract in County and Private Hospitals. C. A. Bachhuber, Los Angeles.—p. 203.
Treatment of Varicose Veins. S. H. Babington, Berkeley, Calif.—p. 208.
Auriculoventricular Block in Pregnancy. A. W. Diddle, Iowa City.—p. 220.
Maternal Mortality and Forceps. F. A. La Breck, Eau Claire, Wis.—p. 225.
Iodine Content of Normal Human Thyroid Gland and Its Correlated Histology. J. D. King and F. E. Hamilton, Columbus, Ohio.—p. 231.
Pregnancy and Syphilis: Résumé of Ten Years Work by the Los Angeles Maternity Service. B. J. Hanley and Lola Pedlow, Los Angeles.—p. 247.

49:259-308 (May) 1941

Back Disabilities Due to Strain of Multifidus Muscle: Cases Treated by Novocain Injection. W. K. Livingston, Portland, Ore.—p. 259.
*Acute Pancreatitis: Thirty-Five Cases with Observations on Blood Amylase Studies. G. K. Rhodes, San Francisco.—p. 266.
Surgical Management of Chronic Duodenal Ulcer. C. T. Sturgeon, Los Angeles.—p. 271.
Problem of Common Duct Stone. J. H. Woolsey, Woodland, Calif.—p. 277.
Instrument for Retraction of Viscera During Peritoneoscopy. S. Robinson and L. G. Fiske, Santa Barbara, Calif.—p. 284.
A Family with Hemolytic Icterus. H. H. Searls, San Francisco.—p. 294.
Present Status of the Newer Urinary Antiseptics. H. A. R. Kreutzmann, San Francisco.—p. 299.
Proximal Y Anastomosis for Treatment of Jejunal Ulcers. M. E. Steinberg, Portland, Ore.—p. 301.

Acute Pancreatitis.—Clinical and experimental studies, according to Rhodes, suggest that several etiologic factors, singly or combined, produce acute pancreatitis. Its etiology in many instances is associated directly or indirectly with disease of the biliary tract. External trauma was the direct etiologic factor in 5 of the author's 35 patients. Severe pain is always present and usually develops from two to three hours after a heavy meal or follows overindulgence in alcohol. Vomiting is a prominent symptom and often precedes pain. Abdominal distention may develop early, and tenderness over the pancreas is the rule. Signs of peritonitis are most evident in the upper quadrants. Physical signs of shock, rapid pulse, lowered pressure and others probably result from the histamine-like protein absorption and are observed only in patients whose gland is extensively involved. Temperature varies from subnormal to a moderate rise. Hyperglycemia and glycosuria depend on the extent of damage to the gland. Diastase in the urine has been used as a diagnostic test, but blood amylase readings probably give more reliable data and are elevated earlier. The rise in blood amylase values is probably the result of absorption of secretions from the obstructed ducts or the absorption of disintegrated pancreatic tissues. Among more than 195 blood amylase determinations it was noticed that the determinations were of most value during the early onset of the disease and that they fluctuated widely within a few hours. After the first twenty-four hours the readings may temporarily be subnormal; it is advisable, therefore, to make frequent determinations. The test is of inestimable value in arriving at a diagnosis of acute pancreatitis. Prior to blood amylase studies the diagnosis was difficult. It was most often confused with perforated peptic ulcer, acute intestinal obstruction and acute cholecystitis. In most instances these errors can be avoided by routine roentgenograms which show pneumoperitoneum, a distended intestine and gallbladder visualization in the respective diseases. The author's experience with 35 patients suggests that during the acute stage of the disease conservatism is the procedure of choice. Most cases undergo spontaneous resolution, even as acute parotitis or acute salpingitis. Surgical intervention when the pathologic process is extensive, as in severe hemorrhagic pancreatitis with obvious surgical shock, is only a heroic gesture. A far better outcome is to be expected if the patient is treated conservatively with transfusions and supportive therapy. Many patients have thus survived the acute initial period and the process has resolved into an abscess or cyst, making the surgical problem relatively simple. At some future date any associated disease of the biliary tract should be eradicated as a prophylaxis against future attacks.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

1:501-544 (April 5) 1941

Rehabilitation of the Injured. E. A. Nicoll.—p. 501.
*Pulmonary Concussion ("Blast"). G. R. Osborn.—p. 506.
Electroencephalography in Traumatic Intracranial Hemorrhage. L. Rogers.—p. 510.
Blood Concentrations Following Local Application of Sulfonamide Compounds to Wounds. F. Hawking and J. E. Piercy.—p. 511.
Pneumococcic Septicemia with Recovery. J. E. Murray and S. Oram.—p. 513.

Pulmonary Concussion.—Osborn compares cases of pulmonary concussion seen in civil life with those resulting from the detonation of high explosives. Among 94 necropsies of persons dying through road accidents there were 8 pulmonary lesions and 3 of these were comparable to bomb cases; these were in girls aged 4 and 8, and a boy of 7. The girl of 4 had been run over by a motor lorry, causing a fracture dislocation of the sixth and seventh cervical vertebrae. Her lungs showed multiple hemorrhages on the pleural surface; they were most numerous in the parts of the lungs which enter the phrenicocostal sinus of the pleura and posteriorly, but there was some rib marking on the lateral surfaces. The liver showed a small laceration of the posterior surface, and there were some peritoneal tears in the transverse colon. The girl of 8 had been knocked down by a motor car; she showed a little bruising over the left lower ribs but was otherwise unmarked. There was a profuse hemothorax from the left and a smaller one from the right side. There was a large tear near the hilus of the left lung, and contusions were scattered throughout both lungs. The liver was torn but the spleen was not. The boy of 7 was run over by a motor lorry. The trunk was not marked. The left lung showed a widespread hemorrhagic lesion about the hilus posteriorly, "rib markings" and a wedge-shaped contusion of the part in the phrenicocostal sinus. In the right lung there were innumerable pinpoint hemorrhages due to inhalation of blood from the left; the spleen showed superficial bruising. The other 5 pulmonary injuries were lacerations from fractured rib ends. The 3 cases in children with flexible chest walls were accompanied by abdominal injuries. Review of road and bomb cases emphasizes the point that there is an abdominal component to the force which produces the basal contusion of the lung. If this wedge-shaped lesion is present the question is not "Is the underlying spleen or liver damaged?" but "How severely is it damaged?" It may be a trivial bruise or a hopeless tear. Most war cases have come from bombed houses and shelters: pulmonary concussion appears to be infrequent in persons injured in an open bombed area. Pulmonary concussion should be looked for in every case from a bombed house. Factors which tend to minimize pulmonary concussion are advancing years, obesity, rigidity of the chest wall, the position of expiration and heavy clothing. So far too little attention has been paid to the fact that the abdomen is suddenly compressed as well as the thorax. Should operation be indicated the organ responsible for the abdominal hemorrhage is likely to be demonstrated by the side of the phrenicocostal sinus lesion. If this is placed posteriorly as well as laterally on the right side the tear in the liver will probably be inaccessible. Tears of the spleen are likely to be at the upper pole. Pulmonary concussion is not necessarily fatal. Death results from acute pulmonary edema and embolism. The latter may be prevented by regular active movements of the lower limbs aided by raising the foot of the bed to prevent hemostasis and by avoiding dehydration and other causes of hemoconcentration. Probably the most important act in treating hemorrhagic concussion of the lungs is to anticipate and prevent pulmonary edema and embolism. Knowledge that the case has occurred in a confined space will help the clinician if he keeps in mind that these patients are prone to suffer from carbon monoxide poisoning (Hadfield and his colleagues). The state of the patient is of greater importance than the size of the bomb or the distance from it. Knowledge of the details of the bomb may be misleading. In houses the positive pressure cannot fall until the walls and the roof are blown open.

Lancet, London

1:471-498 (April 12) 1941

*Wounds of Knee Joint. W. H. Ogilvie.—p. 471.
Idiopathic and Traumatic Narcolepsy. A. W. Gill.—p. 474.
Action of Eserine and Prostigmine on Epileptic Cerebral Discharges. D. Williams and W. R. Russell.—p. 476.
Meningitis with Nasal Disease Due to Streptococcus Viridans. D. R. Cameron.—p. 479.
Hodgkin's Disease in Bladder. R. Phillips.—p. 480.
Staphylococcic Osteomyelitis of Spine. E. C. B. Butler, I. N. Blusger and K. M. A. Perry.—p. 480.

1:499-528 (April 19) 1941

The Modern Troglodyte. Horder.—p. 499.
Fat Embolism. R. A. Rowlands and C. P. G. Wakeley.—p. 502.
Evipan Hypnosis in Psychiatric Outpatients. E. Stungo.—p. 507.

Wounds of Knee Joint.—According to Ogilvie, immobilization of an injured knee until infection has been averted or overcome is the key to successful treatment. In a forward area local treatment is limited to cleansing the skin, applying an abundant sterile dressing and immobilizing the limb for transport. A prophylactic dose of sulfanilamide should be given if possible. Every wound of the knee joint is an urgent case; the most important cases are those seen within the "preinfective" or "grace" period of six hours. Through and through bullet wounds with punctured entry and exit holes do not usually require operation; wounds the result of low velocity projectiles often come in the same category. At time of stress these can be evacuated farther, temporary immobilization being replaced by something efficient and prophylactic sulfanilamide continued. These patients must be watched carefully; the joint must be aspirated if it gets at all tense, and immobilization must be continued until infection is overcome. The early motion of injured joints is as unsound as that of fractures. Most penetrating wounds of the knee joint and all those with injury to the patella or partial injury to the other bones should be operated on. Operation should be done under a tourniquet with the strictest aseptic precautions. Local injuries to bone are treated as radically as possible. A patella splintered by a projectile should usually be removed completely. Holes in the femoral condyles or the articular surface of the tibia may be scraped with a curet or trimmed with a small gouge until they are smooth cavities lined with apparently healthy bone. After excision, suture or partial suture should be attempted. The skin may be closed with interrupted sutures in favorable cases, but if one is in doubt it is better to pack the outer layers of the wound with petrolatum gauze down to the synovial membrane. The only apparatus that gives 100 per cent immobilization of the knee is a plaster spica. Sulfanilamide should be given for a full four days. Dressings are left alone for at least ten days. If evacuation is imperative before this, the surface stitches should be removed and the cutaneous wound packed lightly and left open. Complete fractures of the tibia or femur, seen within six hours of injury, demand primary amputation. After twenty-four hours bacteria have established their entry and the tissues their defenses. The time for débridement is past and the alternatives are expectancy or drainage. The wise policy is to continue immobilization and sulfanilamide, watch the condition of the patient and the wound, aspirate the joint if need be, and be ready to drain or to cut down on a foreign body. As soon as septic infection has been recognized, the knee should be drained, the drainage incisions packed with petrolatum gauze and the whole limb (including the foot and pelvis) immobilized in a closed plaster hip spica. If the infection is overcome within four days the joint is saved, as the cartilage has not been affected; if not, joint and cartilage are lost. If all goes well, the cast should be left undisturbed for at least three weeks; if the patient is not better at the end of four days it is best to amputate the leg. Only complete immobilization will insure success. Changes of plaster casts because of offensive discharge can usually be obviated by fluffed gauze applied over the petrolatum packs and covered by one or two layers of wool firmly bandaged. The cast should be so constructed that its strongest strut is away from the wound. These measures will protect the plaster and, if the rest of the cast is unpadded, will not interfere with immobilization.

Schweizerische medizinische Wochenschrift, Basel

71:149-168 (Feb. 15) 1941

Physiopathology of Asthmatic Crises. A. Epstein.—p. 149.
Osteochondritis Deformans Juvenilis. F. Jakob.—p. 152.
*New Data on Vitamin P. V. Vacek.—p. 155.
Sulfathiazole in Treatment of Swine Erysipelas in Man (Erysipeloid). G. Peyer.—p. 159.
Treatment of Reinfected Tuberculous Fistulas: Case. M. Wasserfallen. p. 159.

Vitamin P.—Vacek studied the effect of vitamin P on capillary resistance, blood clotting time and thrombopenia in a limited number of patients and controls. Capillary permeability was determined in normal subjects with reduced capillary resistance and in persons with hemorrhagic diathesis both before and after injection. Twenty milligrams of a vitamin P preparation was intravenously administered and its effects were noted at intervals of thirty, sixty, one hundred and twenty and one hundred and eighty minutes. The author found that capillary resistance was considerably reduced. Maximal effects were seen in 4 cases after one hour, in 2 after thirty minutes and in 1 case after two hours. The effects wore off after three hours. Blood coagulation time was studied in subjects with normal or slightly protracted clotting times. Vitamin P was seen to accelerate the beginning and termination of coagulation and thus to curtail, on an average, the clotting time by from 20 to 30 per cent. Its effects lasted four hours. No significant effect was observed on the thrombocytic count or on bleeding time in normal subjects. In two cases of purpura haemorrhagica, vitamin P was able to control at least the manifestation of the disease and enable the patient to weather the acute attacks. Two subjects with ulcerative colitis were greatly improved by abundant use of the vitamin. Its therapeutic value was also seen in cases of gingivitis. The author does not attempt to explain the pharmacodynamic mechanism of vitamin P except to note that its effect does not depend on the number of blood platelets. He found that in controls with a normal thrombocytic count petechiae developed when tests for capillary fragility were made before the injection of vitamin. In thrombopenic subjects, while vitamin P did not increase the blood platelets, petechial manifestations either disappeared or did not occur. Vitamin P may, however, influence the blood platelets by strengthening their functional energy.

Giornale Ital. di Dermatologia & Sifilologia, Milan

81:925-1152 (Dec.) 1940. **Partial Index**

*Bactericidal Power of Blood in Course of Staphylococcus Toxoid Treatment. A. Coppolino.—p. 969.

Staphylococcus Toxoid Therapy.—Coppolino made determinations of the bactericidal quality of the blood of 10 patients with staphylococcic infections of the skin before, during and after inoculation with staphylococcus toxoid. Toxoid diluted in the proportion of 1 to 10 parts of physiologic solution of sodium chloride was administered in doses of 0.2, 0.4, 0.6, 0.8 and 1 cc. of the solution. The injections were given at intervals of three or four days. Failure of the first series of injections occurred rarely and only in cases of acute involvement. It was followed by administration of a second series in which undiluted toxoid was used. The studies concerned Staphylococcus aureus of only one strain the virulence of which had previously been determined. The blood was withdrawn when the patients had no fever. The Janneney-Cator method in which citrated blood is used was resorted to in determining the bactericidal power of the blood. The author found that toxoid therapy stimulates production of antitoxins with consequent increase in the bactericidal quality of the blood which is paralleled by clinical improvement. The immunity depends on the dose of toxoid administered in relation to the number of bacteria in the blood. Moderate infection is controlled with diluted toxoid. Undiluted toxoid is indicated in cases of acute involvement in which the bactericidal power of the blood does not change in the course of or after diluted toxoid therapy. An increase in the bactericidal power of the blood in the course of toxoid treatment suggests a good prognosis. The treatment is well tolerated and does not cause local or general untoward reactions.

Revista Mex. de Cir., Ginec. y Cancer, Mexico City

9:39-80 (Feb.) 1941. **Partial Index**

*Blood Transfusion in Puerperal Infection. J. Camarillo.—p. 39.

Blood Transfusion in Puerperal Infection.—According to Camarillo a single blood transfusion in the amount of 100 or 150 cc., administered early in the course of puerperal infection, in association with sulfanilamide controls the infection. Sulfanilamide alone may fail. Transfusion is administered directly from the donor in amounts of 3 cc., with brief interruptions, until 30 cc. of blood has been transfused, after which 10 cc. is given and repeated at brief intervals until 100 or 150 cc. has been transfused. Transfused blood has biophylactic properties by means of which the infection is controlled. The technic is simple and the equipment within reach of all physicians. The author obtained gratifying results from the combined treatment in the maternity department of the General Hospital of Puebla City.

Deutsches Archiv für klinische Medizin, Berlin

186:225-328 (May 6) 1940

Observations on Orthostatic Coronary Insufficiency and Its Nosologic Position. H. Lauer.—p. 225.
Investigations on Normal Form of Electrocardiogram in Lead from Left Leg to Absolute Cardiac Dulness. H. Mössmer.—p. 241.
Investigations on Experimentally Produced Purpura. A. Heymer, J. Hermkes, W. Pfeiffer and J. Spitzer.—p. 258.
Morphologic Observations on Reticulum of Hemopoietic Tissue. W. Tischendorf and A. Frank.—p. 272.
Thoracic Pulsations Accompanying Heart Action. G. Landes.—p. 288.
*Clinical Contribution to Stenosis of Aortic Arch. H. Franke.—p. 304.

Stenosis of Aortic Arch.—Franke defines as stenosis of the aortic isthmus constriction of that part of the aorta located between the branching off of the left subclavian artery and the junction of the ductus arteriosus botalli. The three recognized forms of isthmus stenosis are (1) the typical isthmus stenosis at the orifice of the ductus arteriosus botalli, (2) the isthmus stenosis above and (3) the isthmus stenosis below this orifice. Exact localization is generally not possible during life. Stenosis of the aortic isthmus is rare (0.8 per thousand at necropsies) and stenosis of the aortic arch is extremely rare. The world literature contains reports of only 5 such cases. In this extremely rare type the stenosis is in the arch of the aorta between the branching off of the innominate artery on the one hand and the left common carotid and the left subclavian arteries on the other. The authors recently observed a patient in whom they were able to diagnose stenosis of the aortic arch during life. The high blood pressure in the right arm with great amplitude and pulsus celer et altus in the right radial artery, contrasted with reduced blood pressure in the left arm and the lower extremities with a pulsus parvus and tardus, suggested a mechanical obstacle between these two vascular spheres. Syphilitic genesis of the stenosis could be excluded. There were time differences between the left and the right radial pulse, and the left arm was colder than the right. The main blood stream passed through the greatly dilated innominate artery. The right common carotid artery showed forcible pulsation in contradistinction to the left, which was extremely thin. Even the retinal vessels showed differences in blood perfusion. Percussion disclosed hypertrophy of the left side of the heart. A loud and palpable systolic sound was transmitted into the right carotid and into the right subclavian arteries and often prevented sleep. Persistent right-sided headaches and the development of general signs of intracranial pressure, such as choked disk, increased spinal fluid pressure and bradycardia, suggested a space-consuming process in the cranial cavity. The sudden development of visual disturbances, spastic paralysis of the left leg and a tendency to clownish jokes suggested a frontal brain lesion, probably a cerebral aneurysm, a frequent complication of isthmus stenosis. Diagnosis of stenosis of the aortic arch was corroborated by roentgenologic signs. In the oblique diameters the arch appeared extremely narrow. Dilatation of the right common carotid artery and of the innominate arteries produced displacement of the trachea to the left. The heart, particularly the left ventricle, showed dilatation. Necropsy revealed an aorta with a small diameter throughout and particularly narrow between the innominate and the left common carotid arteries. Necropsy also revealed a cerebral aneurysm and aneurysmatic dilatation of the coronary arteries.

Klinische Wochenschrift, Berlin

19:457-488 (May 18) 1940

New Opinions About Regulation of Respiration. T. Benzinger.—p. 457.
Bound Ascorbic Acid in Plants. P. Holtz and C. Reichel.—p. 461.
Catamnestic Data on Patients with Diabetes Mellitus Treated at Rostock Clinic During Last Ten Years. O. Laur and F. Meythaler.—p. 463.
Hydrochloric Acid-Collargol Reaction as Diagnostic Aid if Cerebrospinal Fluid Specimen Contains Blood. Annelene Kröger.—p. 468.
*Experiences with Protamine Zinc Insulin and Depot Insulin of Bayer. R. Schramm.—p. 470.
Toxicology of 4,4-Dioxy-Alpha, Beta-Diethyl Stilbene. H. Kreitmair and W. Sieckmann.—p. 474.
Does Blood Platelet Count Decrease in the Aged? A. Heymer and G. Ottowess.—p. 478.
Shortening of Coagulation Time of Blood by Means of Oxalate. H. Druckrey and R. von Goeldel.—p. 480.

Protamine Zinc Insulin and a New Depot Insulin.—Schramm states that recently a new method has been developed in preparing a so-called native insulin isolated from the insular apparatus of fresh pancreas which is reported to exert depot-like action without any addition of proteins. The active constituent of this "depot insulin" is a complex which has a protracted blood sugar-decreasing effect. It is the physiologic storage form of the pancreatic hormone in the organism, which is slowly changed into the active form; this makes the depot action of this so-called native insulin understandable. The author made clinical experiments to determine whether this insulin produces the same therapeutic results as does protamine zinc insulin. He found in a group of 80 cases that the same effects can be produced with the depot insulin as with protamine zinc insulin. It was possible to give the two in the same doses in equally severe cases and with the same time arrangement of carbohydrate feedings. The depot insulin has the added advantage in that it contains no protein. The cutaneous reactions are not more frequent and the effect on the blood sugar not inferior to that of protamine zinc insulin. The administration of large doses is possible in some cases but is not successful in all cases of severe diabetes. In a few cases it was possible to compare the actions of protamine zinc insulin and the depot insulin with that of an older form of depot insulin. The first two always proved superior, particularly as regards the distribution of carbohydrates, because they do not require a crowding together of the carbohydrate foods and thus permit greater freedom in the diet. The author reasons that it should be possible to begin insulin therapy with depot insulin, but so far he has accomplished this in only a few cases. For the patient, the immediate treatment with depot insulin would be an advantage because hospitalization could be shortened and the difficulties of transition from one type of insulin to another could be done away with.

Monatsschrift für Kinderheilkunde, Berlin

82:283-430 (April 22) 1940. **Partial Index**

*Simultaneous Appearance of Abacterial Meningitis and Encephalomeningitis or Encephalomyelomeningitis. H. G. Huber.—p. 283.
Studies on Vaccination: Role of Reaction Capacity of Organism in Smallpox Vaccination. D. Gyüre.—p. 304.
Pemphigus Acutus Febrilis in Infants: Report of Four Cases. Helene Sonnemann.—p. 323.
Bacteriology and Immunobiology of Pneumonias in Relation to the Results of Clinical and Immunobiologic Research. Joppich.—p. 329.
Importance of Carbon Dioxide for Forms of Blood Calcium. G. O. Harnapp.—p. 341.
Importance of Anorganic Phosphate for Forms of Biologic Calcium. G. O. Harnapp.—p. 352.

Abacterial Meningitis and Encephalomeningitis.—Huber reports the clinical histories of 11 children aged 2 to 11 years who presented disturbances that must be regarded as manifestations of acute infectious encephalitis of an unknown causal agent. Some of the children presented aspects of so-called idiopathic aseptic meningitis; in others the meningitic symptoms were subordinated to encephalitic symptoms, and 1 child manifested signs of encephalomyelomeningitis. Simultaneously with these disorders in the central nervous system, serous meningitis was observed with increased frequency in adults between the ages of 18 and 35. In all the adults the disease took a favorable course, but 2 of the 11 children died. This indicates that, although the acute infectious encephalomeningitis usually pursues a benign course, it does not always end as favorably as is generally believed. The observations further indicate that the so-called idiopathic aseptic meningitis may be associated with acute encephalitis and that some cases regarded as acute aseptic meningitis *sui generis* probably should be interpreted as manifestations of acute infectious encephalitis.

Wiener medizinische Wochenschrift, Vienna

90:995-1028 (Dec. 28) 1940

Diagnostic Aspects of Postoperative Peptic Ulcer. R. Paolucci.—p. 995.
*Electric Shock Therapy. H. Cerletti.—p. 1000.
Therapy in Cases of Severe Cardiac Decompensation. C. Gamna.—p. 1006.
*Diagnosis of Primary Cancer of Head of Pancreas. A. Gasbarrini.—p. 1009.
Scoliotic Sciatica as Reflex in Protrusion of Intervertebral Disk. V. Putti.—p. 1016.

Electric Shock Therapy.—Cerletti reviews the status of the electric shock therapy of mental disorders. Experiments with different species of animals (dogs, cats, hogs) induced him to try the procedure on human subjects. He learned that it is much less dangerous to pass the electric current through the brain than through the trunk, because in the latter passage the heart is affected. His aim was to find a substitute for the metrazol shock therapy of schizophrenia. Convulsions are elicited with a current voltage of from 70 to 110 (300 to 600 milliamperes). The majority of investigators agree that this voltage is best, but some have employed voltages up to 150. The author passes the current for one tenth of a second, though some investigators pass it for longer periods. The variations in voltage and time indicate that the method has wide limits of tolerance. The number of convulsions necessary to obtain a therapeutic result varies greatly, depending on the type of disease and the individual case. In cases of melancholia and manic depressive psychosis complete recovery has been obtained by from four to six applications. The treatment must not be terminated too early. At the author's clinic the electric shock treatment is usually applied two or three times a week; in other clinics it is given more frequently. Comparisons with the insulin shock therapy revealed that the electric shock therapy is preferable in all mental disturbances accompanied by depression, especially in those patients with psychomotor inhibition or retardation. The author employs it in the majority of patients with schizophrenia. Insulin shock is preferable in patients who are in a state of psychomotor excitation and who are emaciated. In schizophrenia and in manic depressive psychosis recurrences are likely and treatment should be repeated as soon as signs of relapse appear. Braunmühl suggested that in mental disorders of a periodic nature the electric shock therapy be repeated from time to time in order to prevent recurrences.

Diagnosis of Primary Carcinoma of Head of Pancreas.—According to Gasbarrini, primary carcinoma of the head of the pancreas has no characteristic symptomatology. The pain is not intense during the early stage but later may become so severe as to direct attention to the pancreas. The pain is pressing or lancinating and is most frequently located in the epigastric and the umbilical region. The pain may be crisis-like in the beginning and may simulate biliary colic with radiation toward the right shoulder. It may radiate into the lumbar region and toward the left shoulder. Gastrointestinal disturbances are frequent. The patient complains of a feeling of fulness in the epigastrium; he loses his appetite, and an aversion to fats develops. There may be heartburn, nausea, eructation and vomiting. Some patients have a characteristic postprandial borborygmus. There may be intestinal disturbances such as constipation or diarrhea, with an increase in the quantity of feces as the result of deficient digestion and absorption. Fever may be absent or remittent. Cachexia is definitely pronounced. Icterus develops in 90 per cent of the cases. Dilatation of the gallbladder is of considerable diagnostic significance. The author does not agree with Bard and Pic that the liver is always contracted in carcinoma of the head of the pancreas. The spleen is rarely enlarged as long as there is no obstruction in the region of the portal vein. The pancreatic tumor is rarely palpable, but a resistance in the epigastrium is perceptible. Palpation is often made difficult by ascites, meteorism or tenseness of the abdominal wall. As has been urged by Riva and by Zoja, palpation should be done on the fasting patient, when the diges-

tive tract is empty and while the patient is completely relaxed in a warm bath. Roentgenologic examination is valuable. Although the pancreas itself is difficult to visualize, indirect symptoms, which indicate an enlargement of the pancreas, are important. The lesser curvature of the stomach, the antrum and the pylorus show abnormal outlines. The duodenum may show stenosis, lateral deviation, lengthening or the still more characteristic C shape. The transverse colon likewise may exhibit symptoms of deviation and compression. Icterus may be followed by symptoms of compression of the portal vein (ascites) or of the vena cava (edema of the lower extremities, the genitalia, the abdominal wall). Functional disturbances of the digestive tract are frequent and are most important for the diagnosis. Steatorrhea is frequent. The fatty stools contain large quantities of neutral fats and fatty acids but few saponins. The study of the digestive process and of fat elimination permits an estimation of the severity of the pancreatic damage. Tolerance tests with fat may reveal the closure of the pancreatic duct in cases of primary carcinoma of the head of the pancreas. The endocrine disturbances characteristic for diabetes mellitus are rare in pancreatic cancer; however, glycosuria, particularly if it is transitory, may be of considerable importance. Lack of indican is of no particular significance. The differential diagnosis must consider stone in the common duct, chronic pancreatitis with icterus, pancreatic calculi, pancreatic cysts and primary carcinoma of the duodenum, of the ampulla of Vater or of the choledochus. The prognosis of primary carcinoma of the head of the pancreas is unfavorable; the course is comparatively rapid. Surgical treatment has proved ineffective even if employed during the initial stage.

Zeitschrift f. d. ges. Neurol. u. Psychiatrie, Berlin

169:471-606 (May 22) 1940. **Partial Index**

*Theory and Practical Evaluation of Colloidal Gold Reactions. F. Duensing.—p. 471.
Significance of a Certain Type of Encephalographic Ventricle Picture. J. Hempel.—p. 522.
Cerebral Influence on Vegetative Nutritional Rhythm. H. Regelsberger.—p. 532.
"Endocrine-Vegetative" Attacks and Their Relation to Hereditary Epilepsy. J. Schottky.—p. 543.

Colloidal Gold Tests.—Duensing sought to determine the precipitating agent in the colloidal gold reaction by investigating the albumin and globulin fractions in both normal and pathologic spinal fluids. His conclusion is that the precipitation is due to the globulins found in the pathologic fluid and that the difference in spinal fluid findings observed in different nervous diseases may be due to the passage of varying amounts of serum albumins into the cerebrospinal fluid. He enhanced the normal albumin levels by ultrafiltration so that they reached the levels found in the spinal fluid of subjects affected with paralysis, multiple sclerosis and meningitis only to discover that the precipitating effect was negative. This seemed to indicate that considerable qualitative differences exist between the albumins in normal and in pathologic spinal fluids. Examination of the globulin fraction of normal spinal fluid by means of a special (described) method demonstrated that globulins of normal fluid possessed either no coloring power or only an inconsiderable one. It appeared that neither the low albumin content nor the relatively low globulin content in the normal fluid is responsible for the negative colloidal reaction but that the globulins of normal spinal fluid possess some special properties which are either incapable of reacting to colloidal gold or can do so in only a very limited way. On the other hand, the precipitating effect of pathologic fluid was found to be due not to larger concentrations of albumins than are found in normal fluid but to the presence of globulins possessing other colloidal-chemical qualities. However, no disease specificity can be ascribed to globulins since the globulin fraction presented the same characteristics for diseases etiologically different and considerable qualitative variation could be observed in the globulins in different cases of the same disease. Transitional phases of all kinds were observed to exist from nonprecipitating globulins of normal spinal fluid to precipitations of greatest strength found in paralytic fluid. This difference in precipitation is due to the degree of dispersity; globulins which induce a weak precipitation seem to possess a finer dispersity. The albumins in the spinal fluid in cases of diseases of the brain and spinal marrow may be derived, he believes, from the blood serum with the aid of the meninges and the mechanism responsible for the secretion of the cerebrospinal fluid.

Kekkaku, Tokyo

19:1-58 (Jan.) 1941. **Partial Index**

*Studies on the Nature of the Antigen in Complement Fixation Reaction of Tuberculous Serum. S. Kawakami.—p. 1.
*Studies on Nucleinemia. S. Mori.—p. 50.

Tuberculous Antigen in Complement Fixation.—One of the advantages in the performance of the Kogami-Kawakami complement fixation test in tuberculosis, according to Kawakami, is the uniformity in the antigenic activity of the antibodies prepared by the adsorption technic. The antigenicity of the material prepared from tubercle bacilli was found to be approximately the same whether the organisms were grown in Long's synthetic medium or in ordinary glycerin-bouillon medium. Moreover, by the adsorption technic the antigenic property may be unified irrespective of either the strain of the organisms or the medium employed for their culture. In other words, the nature of the tuberculous antigen is influenced by the autoinhibitory substances, and an antigen of uniform activity can be prepared by reducing the inhibitory factor to its minimum level. For the complement fixation reaction the maximum antigenic activity of the tubercle bacilli can be obtained from a culture grown for six weeks or longer on glycerin-bouillon medium. It was found too that lowering of the hydrogen ion concentration (acid reaction) reduces the inhibitory power of the antigen prepared from the dried and powdered bacilli. When the antigens obtained from the bacilli grown on Long's synthetic medium and on 4 per cent glycerin-bouillon were compared by the complement fixation method in 118 serums of tuberculous patients, the former gave 68.6 per cent and the latter 88.1 per cent positive reactions. When the inhibitory factors were eliminated by the adsorption technic, the antigens prepared from the two culture methods gave exactly identical results (91.5 per cent positive). The inhibitory factors present in the antigens can be completely removed by repeated washing with distilled water and by heat desiccation.

Nucleinemia and Erythrocyte Sedimentation.—Thymonucleic acid, a tetranucleotide, is an electrolyte of great molecular weight whose reactions within the living cell with protein, amino acids, ammonium, sodium and hydrogen control such phenomena as the nuclear osmotic pressure, Donnan's equilibriums, water metabolism and nuclear morphology. When the nucleotide or its compounds escape into the blood in abnormal amounts the condition is designated as nucleinemia. Mori believes that nucleinemia is one of the conditions that cause the acceleration of erythrocyte sedimentation rate, and therefore the simple qualitative ring test for the thymonucleic acid level of the plasma offers a convenient method of ascertaining the activity of any disease in which erythrocytic sedimentation is increased. The ring test that the author devised is based on the nucleic reaction of Feulgen (1917), which is the color reaction produced by Schiff's reagent after the hydrolysis of thymonucleic acid. The test is conducted as follows: Exactly 0.2 cc. of either hemolysis-free serum or plasma is mixed with 0.1 cc. of 15 per cent sulfuric acid and heated in a water bath at 80 C. for five minutes. After cooling under the tap, 0.1 cc. of twice normal sodium hydroxide solution is added and the mixture kept at ice box temperature for twenty minutes; after the contents are transferred into a clean small tube, approximately 1 cc. of fuchsin-sulfite reagent is poured on gently to overlay the hydrolyzed serum. After thirty minutes in the refrigerator a violet ring appears at the junction of the two fluids; the density of the color is proportional to the concentration of the thymonucleic acid content of the serum. The author produced necrosis of the tissue in rabbits by subcutaneous injection of 20 cc. of 10 per cent solution of sodium chloride and found that the nucleic acid content of the blood of treated animals roughly parallels the degree of necrosis in the tissue cells. Within thirty minutes after its intravenous injection, the blood concentration of thymonucleic acid begins to lower until, within two hours, it reaches a normal level.

Vrachebnoe Delo, Kharkov

22:401-480 (No. 6) 1940. **Partial Index**

*Question of Universal Donor. V. N. Shamov.—p. 403.
Isohemoagglutinating Properties of Placental Blood. P. M. Rosenberg. —p. 409.
Hemolytic Shock. S. V. Polikarpov.—p. 411.
Symptomatology and Therapy of Frostbites. S. S. Girgolav and T. Ya. Aryev.—p. 415

Universal Donor.—The question of safety of blood transfusion from universal donors is of immense importance for emergency surgery and still more so for military surgery, according to Shamov. Levine and Mabee, Freeman and Whitehouse, Landsteiner and Coca in the United States and Küttner, Schiff and Wildegans in Germany consider this procedure hazardous and counsel against it. In support of their contention these authors cite statistics as to reactions following such transfusion. The author points out that this view is far from being unanimous. Thus, Tzanck in France, Brines in the United States, Moureau in Belgium and Spasokukotsiy and the author in the Soviet Union do not share this view. The author's own statistics from the Kharkov Institute for Blood Transfusion show that in a series of 1,143 transfusions among compatible groups there were 10 per cent severe and 30.7 per cent mild reactions, while in a series of 688 transfusions of blood from universal donors there were 13 per cent severe and 22.1 per cent mild reactions, not a significant difference. The Leningrad Institute for Blood Transfusions, now under the direction of the author, reports a series of eighty-five transfusions from universal donors with 14.1 per cent of mild, 9.4 per cent of moderately severe and 2.3 per cent of severe reactions. The incidence of reactions from transfusion of compatible blood was about the same. The objection raised against the use of the blood of universal donors is the presence of agglutinins α and β in their serum. It is argued that, if this titer is high and the recipient is very anemic, agglutination of red cells of the recipient and hemolysis might take place. The author points out that this so-called reversed agglutination cannot explain reactions taking place after transfusions of such small quantities of blood as 3, 5, 20 or 50 cc. He also points to Moureau's experience in giving 8 persons transfusions with blood from universal donors in amounts as high as 650 cc., the donors' blood containing a titer of from $\frac{1}{16}$ to $\frac{1}{102}$ against agglutinogen α without any complication being noted. Samples of blood taken from the vein of the opposite side of the recipient in the course of the transfusion did not contain a trace of these agglutinins. The author believes that there exists some special mechanism for neutralization of the agglutinins besides the mere factor of dilution of the transfused blood. This mechanism may be found in the mass of agglutinogens contained not only in the erythrocytes but also in the plasma and the viscera of the recipient. The author concludes that transfusion of blood from universal donors is not associated with greater hazards than that of compatible blood. The acceptance of this opinion should be of importance to the solution of the problem of transfusion in the field of military action.

Nordisk Medicin, Stockholm

9:81-162 (Jan. 11) 1941. **Partial Index**

Hospitalstidende

*Hyperparathyroidism: Two Cases Treated Operatively with Remarks on Geographic Distribution. H. E. Nielsen and K. Steffensen.—p. 115.

Hyperparathyroidism.—In the first of Nielsen and Steffensen's 2 cases of hyperparathyroidism due to adenoma, in women aged 57 and 43 respectively, with onset of symptoms at 48 and 40, the combination of renal calculus and calcium atrophy together with rheumatic-like pain in the extremities suggested the parathyroid disorder, while in the second case admission for treatment because of spontaneous fractures led to the diagnosis. In the first instance psychic changes were seen, manifested by alterations in character. In both cases roentgen examination showed osteomalacia and cyst formation. There were hypercalcemia and hypophosphatemia in the first case, considerable increase in the blood phosphatase in both cases. Complete recovery occurred in both cases after removal of the adenomas. In 1 case the postoperative course was complicated by a tetany of brief duration, in the other the absence of tetany is attributed to prophylactic treatment with dihydrotachysterol. Examination of the blood phosphatase is especially helpful in cases of hyperparathyroidism of long standing with changes in the bones, since osteitis fibrosa-like changes accompanied by normal serum phosphatase exclude hyperparathyroidism; hypercalcemia is particularly significant in diagnosis in the earlier stages of the disease. They state that about 200 cases of hyperparathyroidism have been reported, 14 of these (including 13 with established adenomas) from Denmark. Adenoma formation is assumed to depend on certain embryonal cells with the power of adenoma formation, which are rarely found in the parathyroid glands and then usually in one gland. The lack of vitamin D or ultraviolet rays is believed to stimulate the parathyroid apparatus with resulting proliferation of these cells and so adenoma formation. The embryonal cells in question are thought to be present equally often in different localities, but adenoma formation occurs more often where there is greater stimulation.

9:163-242 (Jan. 18) 1941. **Partial Index**

Observations Concerning Effect of Sulfonamide and Sulfapyridine Preparations on Pulmonary Tuberculosis. K. A. Vannfält.—p. 163.
*New and Specific Cutaneous Reaction in Boeck's Sarcoid: Preliminary Report. A. Kveim.—p. 169.

New and Specific Cutaneous Reaction in Boeck's Sarcoid.—Kveim found that in patients with sarcoid of Boeck a nodelike thickening of the skin appeared in the course of from one to several weeks after intracutaneous injection of a sterile extract of sarcoid tissue (from gland or skin nodules). The nodule remained for from weeks to months and its microscopic structure was often not to be distinguished from that of spontaneously originated sarcoid nodes. He regards this as a specific reaction of allergic type, since it did not occur in the control cases of lupus and syphilis, and injection with Frey's antigen caused no reaction in patients with Boeck's sarcoid. In his opinion the establishment of this specific cutaneous reaction supports the view that sarcoid of Boeck is a distinct entity.

Ugeskrift for Læger, Copenhagen

103:159-196 (Feb. 6) 1941

*Death from Procaine Hydrochloride, in Connection with Infiltration of Procaine Hydrochloride into the Stellate Ganglion. J. L. Hansen. —p. 159.

Death from Procaine Hydrochloride.—In Hansen's case, in a woman aged 62 with a history of severe bronchial asthma for sixteen years, resistant to treatment, extirpation of the stellate ganglion was contemplated. Preliminary infiltration of the ganglion by injection by the posterior route of from 20 to 80 cc. of a 1 per cent solution of procaine hydrochloride without epinephrine was done five times in the course of twenty days, each injection being given during an attack of asthma, with excellent results. Intravascular injection was guarded against by aspiration tests. On the sixth infiltration 25 cc. (about 0.35 Gm. of procaine hydrochloride) was injected in the usual manner. In the first five minutes the respiration became completely free, then respiratory paralysis set in and in spite of immediate treatment with nikethamide and intracardiac injection of digitalis, together with artificial respiration and careful massage of the heart, death occurred within ten minutes after the injection. Chemical analysis showed that only the pure substance had been used. The author says that in this case, as in most published cases of fatal procaine intoxication, the actual cause of death was not clear, but the primary cause here was probably the infiltration of procaine around the stellate ganglion. He believes that of the factors which may play a part in death from procaine hydrochloride the following, either singly or in combination, may have contributed in this instance: (*a*) faster resorption than usual, (*b*) influence on the vagus, (*c*) cerebral anemia due to perivascular injection, (*d*) transport along the nerves to important centers, eventually on the basis of endoneural injection, and (*e*) reduction of the procaine-eliminating ability of the liver. He urges further investigation on deaths following injections of procaine hydrochloride and the publication of cases which are fatal. He does not warn against blocking of the sympathetic but emphasizes that the procedure calls for strict indications and careful consideration.

Book Notices

Psychotherapy: Treatment That Attempts to Improve the Condition of a Human Being by Means of Influences That Are Brought to Bear Upon His Mind. By Lewellys F. Barker, M.D., Visiting Physician, Johns Hopkins Hospital, Baltimore. Cloth. Price, $2. Pp. 218. New York & London: D. Appleton-Century Company, Incorporated, 1940.

"Treatment that attempts to improve the condition of a human being by means of influences that are brought to bear upon his mind." The promise of a broad and eclectic point of view given by this definition is borne out by Barker's book on psychotherapy. The treatise is not a lengthy one. There are nine chapters, a glossary, a bibliography and an index. The first chapter contributes several adequate descriptive definitions of psychotherapy. The second chapter recounts and describes the steps that are necessary in order to arrive at diagnostic shaping conclusions; the third indicates how the acquired information may be utilized in forging effective psychotherapeutic weapons; the fourth chapter suggests the particular trends that may be imparted to psychotherapy by reason of a scrutiny of heredity and environment. The fifth chapter discusses in fifty-one pages more than fifteen methods of psychotherapy. The chapter reveals both the assets and the defects of Barker's contribution. About a half of these discussions, though quite brief, are nevertheless stimulating enough to excite further interest and study. However, whenever conclusions are given there is the danger of inviting misinterpretation and misconception resulting from inadequacy of discussion. For instance, the remarks concerning psychotherapy in alcoholism do not give any indication concerning the considerable progress which has been made in the identification and understanding of alcohol habituation as a psychoneurosis resulting from emotional immaturity determined in childhood. A short chapter on the psychotherapy of so-called organic diseases emphasizes the psychotherapeutic significance of the now commonly accepted doctrine of the fundamental unity of man; the entwining of physical and psychic; the constant interchange between structural and emotional reactions. The seventh and eighth chapters focus on psychotherapy from the angles of the particular psychoneurosis or psychosis which is the target of the therapy and the life epoch in which there occur the problems which psychotherapy attempts to solve. The glossary will be helpful in giving the student a quicker understanding of the subject matter. The bibliography constitutes an excellent reading list. In the final chapter the author gives a glimpse of the fascinating vistas of the therapy which may be unfolded in the future. The author is inclined to believe that "a part of psychotherapy in the future" may "be compelled to give way to new forms of chemotherapy."

Let us hope that there will be not a displacement of one by the other but rather a mutual and deeper understanding, so that both psychic and chemical technics become increasingly effective and the frontal attack on the pathologic defenses of human maladjustments becomes more and more successful.

A Short Practice of Surgery. By Hamilton Bailey, F.R.C.S., Surgeon, Royal Northern Hospital, London, and R. J. McNeill Love, M.S., F.R.C.S., Surgeon, Royal Northern and Metropolitan Hospitals, London. Fifth edition. Cloth. Price, 30s. Pp. 1,015, with 880 illustrations. London: H. K. Lewis & Co., Ltd., 1941.

This is the fifth edition of this book over a period of nine years. At first glance this may appear to be an excessive number of revisions, but comparison with a popular American textbook reveals that this volume had been revised the same number of times over the past decade. These frequent editions are indicative of the rapid changes in the science of surgery, but they also indicate the difficulty of fitting a modern textbook on surgery to the needs of the student. In many respects this book is an excellent summary of clinical surgery. Little or no surgical technic other than the principles of operations is included. Cursory descriptions of clinical diagnostic features and brief pathologic anatomic descriptions are the chief contents. The book begins with some fundamentals of bacteriology essential to the surgeon and with certain specific infectious diseases. It then proceeds to the various surgical problems associated with regional disorders and concludes with an excellent section on orthopedic surgery.

Such a volume is necessarily dogmatic and for the sake of brevity resorts to the outlining of many details. Frequent and excellent illustrations usually supplement any inadequacies in the text. There are numerous photographs and many colored drawings, which the high quality of paper employed flatters to the utmost. This is a feature lacking in many otherwise good surgical textbooks.

It is possible for the student to absorb from this a considerable number of highlights on surgical problems. For thorough study and reference, however, it hardly supplies sufficient information. A bibliography is not included for supplemental study, although brief biographic footnotes are an interesting addition to almost every page. The value of the book lies in its succinct clarity and the attractive style in which it is written. It represents again a typical surgical volume prepared for British students and contrasts clearly with textbooks used in this country.

The Mask of Sanity: An Attempt to Reinterpret the So-Called Psychopathic Personality. By Hervey Cleckley, B.S., B.A., M.D., Professor of Neuropsychiatry, University of Georgia School of Medicine, Augusta. Cloth. Price, $3. Pp. 298. St. Louis: C. V. Mosby Company, 1941.

As a psychiatrist in the United States Veterans Administration the author became interested in that nosological wastebasket known as "psychopathic inferiority" and its minor diagnostic variations. He has given much thought to these conditions and has set forth his studies and conclusions in a serious and scholarly work. Cleckley has a flair for the literary, so that in spots he romanticizes his subject and in places he has recourse to the technic of sensational reporting; but these passages need not divert the reader from an extremely worth while account of the subject of psychopathic personalities. The difficulties of treating these patients under our existing insanity codes is thoroughly presented and their prevalence estimated. The author then presents fifteen detailed and illuminating case histories He summarizes existing opinion regarding the group, differentiates it from other entities and sharply outlines and circumscribes the clinical syndrome. Finally he attempts an interpretation of the clinical process and discusses therapy. Use is made of dynamic concepts, and a good grasp of the basic problems is evidenced by the author. He uses the term semantic dementia as indicating a loss of grasp or utilization of the significance or meaning of experience. The book is highly recommended.

Inter-Relation of Abdominal Diseases. By Elemér Forral, M.D., L.R.C.P. With a foreword by Sir Arthur Hurst, M.A., D.M., F.R.C.P., Consulting Physician, Guy's Hospital, London. Cloth. Price, 12s. 6d. Pp. 168, with 5 illustrations. London: William Heinemann, Ltd., 1941.

The author develops the thesis that all the organs of the gastrointestinal and hepatobiliary tracts should be considered as belonging to a single system. This conclusion is based on the fact that they have a common embryologic origin, similar nervous and reflex pathways, the various organs are frequently invaded by identical bacteria and there is often a pronounced familial predisposition to disease of one or more units of this system. These and other factors prove the close interrelationship in a pathologic and clinical sense between various parts of the system and help to explain the frequent coexistence of chronic disease in the gallbladder, appendix, duodenum, stomach and liver. This conception also throws some light on residual symptoms so frequently present after removal of a chronically involved gallbladder or appendix, since several organs or even the entire system are usually involved and removal of the gallbladder or appendix serves only to eradicate but a small segment of the diseased whole. It has been known for some time that peptic ulcer and chronic gallbladder or appendical disease coexist in the same patient, but this is the first time that such a comprehensive view has been offered in explanation of this phenomenon. A careful survey of the literature and a study of the author's own material constitute the basis for his conclusions, which, in addition to the foregoing, also include views on the role of the liver in the production of allergy, on the thyroid and on the significance of heredity in relation to intra-abdominal disease. The critical reader may not agree that all statements made by the author actually support his thesis. Certainly such far reaching conclusions should be checked by a greater series

of controls. But these criticisms in no way detract from the value of this book as a thought provoking and scholarly attempt to explain the troublesome failures which so frequently follow medical and surgical treatment of chronic disease of the digestive tract.

Hæmorrhoids and Their Treatment: The Varicose Syndrome of the Rectum. By Kasper Blond, M.D. Translated by E. Stanley Lee, M.S., F.R.C.S. Cloth. Price, $4.50. Pp. 140, with 49 illustrations. Baltimore: William Wood & Company, 1940.

The first five chapters are devoted to the etiology, symptomatology, diagnosis, investigation and treatment of hemorrhoids. In twelve years the author has performed 3,100 injections. "In 1935, after some 2,000 cases had been treated without serious complication, there occurred in rapid succession two fatalities." The author calls his treatment the "vein compression method and it consists of injections of about 8 minims of 20 per cent solution of quinine bihydrochloride, urethane, procaine and tincture of catechu (20 per cent)." This injection is made "round the bowel in a clockwise sequence, under the mucosa at a level above the hemorrhoids." It is claimed that "the cure is usually complete in five to seven treatments," although one patient "required more than twenty." The author claims that "the fissure owes its existence to a thrombosed varix" and "piles are found in 100 per cent of the cases." He also states that "fistula in ano is a suppurative thrombophlebitis" and that "the underlying cause of fistula is the hemorrhoids." Therefore, he says, "it follows that the treatment of fistula must begin with the treatment of hemorrhoids." In like manner the author deals in remaining chapters with the subjects of constipation, pruritus, proctitis, fistula, prolapse, biliary disease and varicose veins, and each problem is finally reduced to the same common denominator: The cause of the disease is "venous back pressure," and the "venous compression treatment" cures all disorders which occur caudad to the area where the treatment is given. The author admits that many of his ideas are the same as those of the physicians of an early day. It is his idea that the modern physician is in error because he rejects many of the old schemes. The volume consists, in part, of claims and opinions which probably will not find general acceptance. Many of the illustrations are in color.

Growing Out of Babyhood: Problems of the Preschool Child. By William S. Sadler, M.D., F.A.P.A., Chief Psychiatrist and Director, the Chicago Institute of Research and Diagnosis, Chicago, and Lena K. Sadler, M.D., F.A.C.S., Associate Director, the Chicago Institute of Research and Diagnosis. Cloth. Price, $2.50. Pp. 350. New York & London: Funk & Wagnalls Company, 1940.

This book has been prepared particularly for mothers, nurses and governesses and is devoted to the psychologic, psychiatric and sociologic problems of the preschool period. It attempts to furnish parents with definite instructions for dealing with the specific behavior problems that arise during this period. It contains much material collated from a variety of sources. The introductory chapters deal with the normal child, while the largest portion of the book is devoted to the common problems of the preschool period; namely, bowel and bladder training, thumb sucking, nail biting, temper tantrums, obedience and discipline. The latter chapters are concerned with the adjustment of the child to the group and parent-child relationships. While this material is not new, it is well presented, clearly written and should aid parents in correcting behavior problems. Because of the amount of material included, there is some question as to how much of the information and instruction will be grasped by average parents.

Age Morphology of Primary Tubercles. By Henry C. Sweany, M.D., Medical Director of Research, Municipal Tuberculosis Sanitarium, Chicago. Cloth. Price, $5. Pp. 265, with 73 plates. Springfield, Illinois & Baltimore: Charles C. Thomas, 1941.

Based on the idea that practically all biologic phenomena are more or less functions of time, the author has made a rather comprehensive study of primary tubercles. He presents evidence in support of the thesis of the relationship of age to morphology of primary tubercles. He presents the interesting analogy of the aging tubercles to the various changes in the earth which become understandable in the science of geology. The application of "morphology" criteria may be applied practically to approximate the time of contact, the location of the source of contagion in conjugal infection, the relation of the onset of tuberculosis to other diseases. This method may also prove useful in medicolegal work and in government compensation following military or naval service. The author admits the controversial nature of the subject. Further study is necessary to confirm this theory, and it is questionable whether one can go as far as the author has in his deductions.

The Prevalence of Disabling Illness Among Male and Female Workers and Housewives. By David E. Hailman, Senior Administrative Assistant, United States Public Health Service. From the Division of Public Health Methods, National Institute of Health. Prepared by direction of the Surgeon General. Federal Security Agency, U. S. Public Health Service. Public Health Bulletin No. 260. Paper. Price, 10 cents. Pp. 40, with 10 illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1941.

The classification of the data collected by the National Health Survey according to age, employment and sex indicates that the rate of illness as measured by the proportion of persons disabled on the day of the visit was 48 per cent higher for females in the ages 15-64 than for man. The rates for industrial workers in the same age group were 32 per cent higher for males and 17 per cent for females than for those in the business, professional and clerical classes. For cancer and other tumors, nervous and mental diseases, tonsillitis and a number of other diseases, the female rate was much higher than the male, while the male rates were high for hernia, ulcer of the stomach and duodenum, occupational accidents, hemorrhoids and pneumonia. While there were these significant differences between the sexes, the curves of sickness rate for the two sexes in all classes followed much the same pattern.

Corner Druggist. By Robert B. Nixon, Jr. Cloth. Price, $2.50. Pp. 291. New York: Prentice-Hall, Inc., 1941.

The doctors and the dentists and the lawyers and the editors have been writing their autobiographies, and in some instances their sons have been exploiting their careers. Now comes the biography of a corner druggist, written by his son. It is a lively book, and any one who has wasted his hours gossiping with the druggist at night back of the prescription counter, or more recently behind the soda fountain, knows that the druggists have a lively time. Not all of their spare time is spent in selling stamps. The corner druggist, whose story is told here, was a druggist of the old school. Apparently in the old days they were frequently besought to provide pills for removing the premature progeny of seduction; they prescribed for venereal disease, and they advised the family about conditions in general. Modern scientific pharmacy is apparently removing some of the romance from this lively profession, but it is amusing and interesting to read what the druggist of an earlier day contended with.

Trudy Rostovskogo na Donu Gosudarstvennogo Meditsinskogo Instituta. Sbornik IV. Otvetsvenny redaktor: N. A. Bogoraz. [Publications of State Medical Institute of Rostov-on-Don. Fourth Collection.] Paper. Price, 9 rubles. Pp. 216, with 56 illustrations. Rostov-on-Don: Rostovskoe Oblastnoe Knigoizdatelstvo, 1939.

Trudy Rostovskogo na Donu Gosudarstvennogo Meditsinskogo Instituta. Sbornik V. Otvetstvenny redaktor: N. A. Bogoraz. [Publications of Rostov Medical Institute. Volume V.] Paper. Pp. 319, with 103 illustrations. Rostov on Don: Rostovskoe Oblastnoe Knigoizdatelstvo, 1939.

Trudy Rostovskogo Gosudarstvennogo Meditsinskogo Instituta. Sbornik VI. Pod redaktsiey: K. Z. Yatsuta. [Publications of Rostov Medical Institute. Volume VI.] Paper. Price, 12 rubles. Pp. 295. Rostov on Don: Rostovskoe Oblastnoe Vedomstvennoe Izdatelstvo, 1940.

Volumes IV, V and VI of the Publications of the State Medical Institute of Rostov on Don contain a motley of papers on clinical and experimental work reflecting an average standard for medical institutes of the Soviet Union. A review of the material is not possible because of the number and the variety of subjects treated.

National Board of Medical Examiners. Examination Questions. Parts I and II. Revised to October 1, 1940. 1936-1940. Bulletin No. 8. Paper. Price, 25 cents. Pp. 155. Philadelphia, [n. d.].

This compilation of questions used by the National Board of Medical Examiners doubtless fills a want on the part of certain poorly qualified students preparing for this test. Further, it gives aid and comfort to those instructors who permit their courses to degenerate to the level of an examining school. Whether it serves any useful purpose does not appear.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

PULMONARY TUBERCULOSIS AND HOT CLIMATE

To the Editor:—**A woman aged 28, who is being treated for pulmonary tuberculosis (compression has been performed) has greatly improved, being bacillus free and afebrile. She is about to be married. Her prospective husband's occupation necessitates living in the tropics and, at times, on the coast of Peru, where the climate is hot. I should like to know how patients who have been tuberculous can stand the tropics and shall appreciate any information you can give me.**

L. H. Hoffman, M.D., San Francisco.

ANSWER.—There need be no hesitancy in going to a hot climate so long as the treatment of the disease can and will be properly carried out. The patient must have adequate rest for the particular stage of her disease, be kept comfortable and contented and be maintained on a good modern diet. If the collapse is to be continued, it will be necessary to stay near some competent man who can administer it. At Lima there are such men and perhaps these men may be able to recommend others. The only obvious danger is the possibility of having to go to high altitudes with too much lung collapse. This should be done carefully, as an adequate sea level pressure in the pleural cavity may become too great at high altitudes. It would be better to ascend in stages of only a few thousand feet at a time, and only under the care of a competent physician.

CHRONIC SINUSITIS AND PEPTIC ULCER

To the Editor:—**In the past year a patient has had gastric and duodenal ulcers. In 1918 he had an acute infection involving all the sinuses. The condition finally became chronic. There were many acute flare-ups superimposed on a more or less chronically active state. In the fall of 1918 he experienced a loss of the sense of smell and a diminished sense of taste. These losses have never been regained. What effect would the loss of these senses have on normal gastric secretion? Would the continuous swallowing of pus from these sinuses be considered a primary or a secondary cause of gastric ulceration? Would these losses contribute to ulcer formation? From 1918 to 1935 he experienced gastric disturbances. In May 1935, following an acute attack of sinusitis, he had acute gastritis, which subsided under treatment. The condition became chronic. Prior to the development of a gastric ulcer in 1940 he suffered an acute attack of sinusitis.**

M.D., New York.

ANSWER.—The mechanism of normal gastric secretion in response to a meal consists of three phases: the psychic, the gastric and the intestinal. In addition there may be a continuous secretion, variable in amount, which is not dependent on the intake of food. The sense of taste and the sense of smell can influence only the psychic phase of gastric secretion. The volume of gastric juice secreted during the psychic phase may vary considerably from one person to another and in the same person from meal to meal. On the basis of Carlson's (The Control of Hunger in Health and Disease, Chicago, University of Chicago Press, 1916, pp. 232-247) observations it seems reasonable to assume that in general the psychic gastric secretion does not amount to more than one fifth of the total secretion of the stomach and that it might well be less.

Carlson found that "significant appetite secretion in man is that induced by tasting and chewing good food." The secretion of gastric juice produced by seeing, smelling or thinking of food was relatively slight and inconstant. Furthermore, the mere act of chewing (paraffin) was found not to stimulate gastric secretion. This suggests that the sense of taste is an important factor in the production of appetite secretion. It does not, however, indicate that the inability to taste food completely abolishes the psychic phase of gastric secretion.

The effect of the loss of the sense of taste and the sense of smell on the total volume of gastric secretion would seem, therefore, to be at most a slight, probably insignificant, decrease. There is no evidence to indicate that the loss of these senses leads to the formation of chronic peptic ulcers.

Although acute sinusitis, chronic sinusitis and exacerbations of chronic sinusitis have sometimes been mentioned as possible causes of chronic peptic ulcer, this is highly questionable. Whether a patient who has had a peptic ulcer is predisposed to a recurrence by infection of the sinuses or, indeed, by infection anywhere in the body is not known but seems unlikely. It has been stated, but not proved, that persons with peptic ulcers have a higher incidence of chronic infections, including sinusitis, than those who do not have peptic ulcers. Hurst and Stewart (Gastric and Duodenal Ulcer, Oxford University Press, 1929, p. 48) in discussing this subject add, however, that "the clinical evidence for this is not absolutely conclusive, as chronic infections are so common that the possibility of coincidence requires consideration." Considerable coincidence would be bound to occur and, for this reason, such statistical studies are difficult to evaluate.

It might seem reasonable to expect the swallowing of infectious discharges from the sinuses to lead to some changes in the mucosa of the gastrointestinal tract. This may well occur, but it has not been shown that chronic peptic ulcers result. It should be noted that gastric contents with a p_H value of 3 or less have been found to have a bactericidal effect (Hood, Marion, and Arnold, Lloyd: *Am. J. Digest. Dis. & Nutrition* **4**:40 [March] 1937). It is significant, however, that the healing of chronic peptic ulcers in man and similar experimental ulcers in animals is promoted by antacid therapy which maintains the gastric contents at a p_H value above 3 (Palmer, W. L.: Fundamental Difficulties in the Treatment of Peptic Ulcer, THE JOURNAL, Nov. 18, 1933, p. 1604). The gastric flora, which is largely determined by the flora in the oral cavity and the upper part of the respiratory tract, apparently has little influence on the healing of such ulcers.

It would appear, therefore, that infection of the sinuses has no known role in the pathogenesis of chronic peptic ulcers.

TESTOSTERONE PROPIONATE FOR PROSTATIC HYPERTROPHY

To the Editor:—**Will you please give me the consensus as to the usefulness of testosterone propionate in benign prostatic hypertrophy. If of use, what is the recommended manner of use?**

William J. Hall, M.D., McKees Rocks, Pa.

ANSWER.—In the report on this substance by the Council on Pharmacy and Chemistry, the first sentence reads "Within the past few months extravagant claims for the action of the male sex hormone testosterone have appeared in professional and lay publications." This sentence, distinguished by restraint, introduces an excellent review of the literature pertinent to the use of testosterone propionate. The report is concluded by a refusal to include this substance in New and Nonofficial Remedies.

Since the publication of this report in 1939, many articles have appeared concerning the use (and misuse) of testosterone. It has been advised for the treatment of most of the ailments of males, from delayed puberty to old age, from undescended testes to impotence and prostatic hypertrophy, for enuresis and acne. Even females are not exempt, for it is advised in the treatment of many of their complaints, including menorrhagia. From a cursory examination of this mass of prematurely published and poorly considered literature, it might be assumed that in testosterone there is the answer to "all of the acute and chronic diseases of men, women and children."

Actually, testosterone propionate is an excellent substance. It is one of the few pure, synthesized hormones yet made available. It is an extremely valuable substance for the treatment of patients suffering from a lack of this substance—such as those who have eunuchoidism. When all the nonsense written about it is forgotten, testosterone propionate will have an honored place in the medical armamentarium.

In answer to the specific question, it may be said "There is no scientifically acceptable evidence that testosterone is of permanent value in the treatment of prostatic hypertrophy." This statement is made in spite of such enthusiastic claims as those of Trasoff, who reported good results with the substance in 23 of 27 cases of prostatic hypertrophy. The answer is based rather on such excellent work as that of Heckel, who concluded his thorough study by stating:

"Testosterone propionate in daily intramuscular injections produced little improvement in the symptoms and clinical course of 22 patients with benign prostatic hypertrophy.

"It did not produce any noteworthy reduction in the residual urine.

"The histological examination of the prostate gland from the patients who were previously treated with testosterone propionate showed no variation from the histological sections from untreated patients.

"Testosterone propionate produces a temporary depletion of spermatozoa in patients that have spermatozoa counts within normal limits. In 10 of 12 patients an oligospermia was produced.

"These data would indicate that this material is of little benefit in the treatment of benign prostatic hypertrophy, and its promiscuous use over a long period of time in patients with normal testicular function might be harmful."

The lack of any change in the histologic aspects of the gland after therapy with propionate also has been reported by Sharpey-Schafer and Shackman.

Perhaps, in some cases, some subjective improvement has been obtained by such treatment, but, as Heckel wrote, "The benefits that did occur were mild and were no greater than the improvement commonly seen when the patient is prescribed soda and sitz baths. It seems, therefore, improbable that the hormone caused any beneficial effects."

It is more likely that testosterone will have a valuable role in the treatment of underdevelopment of the prostate gland. McCullagh and McGurl reported that "the prostate glands in 6 cases of prepuberal hypogonadism have grown in some cases from almost no palpable prostatic tissue to approximately normal size."

References:

The Present Status of Testosterone Propionate: Three Brands, Perandren, Oreton and Neohombreol (Roche-Organon) Not Acceptable for N. N. R., Report of the Council on Pharmacy and Chemistry, THE JOURNAL, May 13, 1939, p. 1949.

Trasoff, Abraham: Treatment of Benign Prostatic Hypertrophy with Testosterone Propionate, *J. Lab. & Clin. Med.* **25**: 377 (Jan.) 1939.

Heckel, Norris J.: The Influence of Testosterone Propionate on Benign Prostatic Hypertrophy and Spermatogenesis: A Clinical and Pathological Study in the Human, *J. Urol.* **43**: 286 (Feb.) 1940.

Sharpey-Schafer, E. P., and Shackman, R.: Testosterone Propionate: Its Effect on the Histology of Prostatic Enlargement in Man, *Lancet* **1**: 1254 (June 3) 1939.

McCullagh, E. Perry, and McGurl, F. J.: Further Observations on the Clinical Use of Testosterone Propionate, *J. Urol.* **42**: 1265 (Dec.) 1939.

POSSIBLE PULMONARY ASPERGILLOSIS

To the Editor:—**I have a roentgenogram which is suggestive of numerous small, discrete calcified pulmonary lesions with a hematogenic distribution which, on account of the history, suggests infection with Aspergillus. I would appreciate any information or references you can give me with regard to this. Is the condition likely to produce gastric symptoms similar to those occasionally produced by pulmonary tuberculosis?**

Arthur E. Perley, M.D., Waterloo, Iowa.

ANSWER.—With such meager data it is impossible to arrive at a conclusion as to the cause of the discrete dense shadows in the lung as seen roentgenographically. What in the history suggests infection with Aspergillus?

The following information may be offered: Since 1842, when pulmonary aspergillosis was first described, there has been much discussion as to whether the infection is primary or secondary. Primary infection of the lung has been rarely reported by American authors. Generally, writers in this country are loath to accept the theory of primary infection, and many even question the pathogenicity of the fungus under any circumstances. Among European authors, especially the French, primary aspergillosis is accepted as an entity and not infrequently reported as such.

Pathologists in this country concur with clinicians that aspergillosis of man as a primary process is rare, but that as an accompaniment of many pulmonary lesions such as old infarcts, bronchitis (Weidman, F. D.: *Arch. Path.* **13**:725 [May] 1932), bronchogenic carcinoma (Kampmeier, R. H., and Black, H. A.: *Am. Rev. Tuberc.* **30**:315 [Sept.] 1934) and especially pulmonary tuberculosis (Edwards, J. C.: *New England J. Med.* **213**:15 [July 4] 1935) it is not common.

Pathologically the lesions appear essentially as bronchiectasis or edematous necrosis (Weidman). Nowhere in the early literature is mention made specifically of fibrosis and calcification as part of the process. Because of the almost invariable superimposition of aspergillosis on another pathologic entity, at least as noted in this country, any calcification present may have been due to the underlying or primary disease.

In 1932 Sayers and Meriwether (*Am. J. Roentgenol.* **27**:337 [March] 1932) stated that they had isolated Aspergillus from the sputum of 31 patients who had what appeared roentgenographically to be typical healed miliary tuberculosis of the lung. There was no evidence that the fungi present were the cause of the shadows in the lungs. Experimentally produced aspergillosis has never resulted in calcified lesions. Bethune and Moffatt (*J. Thoracic Surg.* **3**:86 [Oct.] 1933), who produced experimental aspergillosis in guinea pigs, rats and rabbits, concluded that there was no evidence to favor the theory that Aspergillus may be responsible for extensive fibrosis and nodular calcification as seen in some roentgenograms of human beings.

The rare clinical cases that appear to be primary aspergillosis also support the pathologists' views. Cannon (*J. Thoracic Surg.* **4**:533 [June] 1935) reported a primary case in which there were relatively slight pulmonary lesions and no evidence of extensive fibrosis or calcification. There has apparently been no reported case of uncomplicated aspergillosis with calcification as a feature.

It is probable that aspergillosis of the lungs, should it be present, would be apt to be accompanied with symptoms of disturbance of the gastrointestinal tract such as may occur in pulmonary tuberculosis.

BLUE SCLERAS AND BRITTLE BONES

To the Editor:—**What is the significance of blue scleras in a 2 year old girl? She is apparently normal. What are the possibilities of her acquiring fragilitas ossium, although there is no other evidence at present? What sort of a check-up (including laboratory methods) should she have? The blue scleras have been present from birth, but the shade of blue has increased in intensity.**

M.D., New Jersey.

ANSWER.—The blue color of the sclera is imparted by the choroidal pigment. Whether this is made possible by an unusual transparency or by thinness of the sclera is a question of mild controversy.

Approximately 60 per cent of adults with blue scleras have brittle bones. About 60 per cent have associated deafness, while in 44 per cent all three conditions may be present (Fox, M. S., and Sweet, S. J.: Brittle Bones Associated with Deafness and Blue Scleras, *Arch. Otolaryng.* **32**:506 [Sept.] 1940).

Brittle bones and blue scleras are associated also with relaxed ligaments and the syndrome is hereditary. It follows the mendelian law of inheritance and is a disturbance of the mesenchyme, from which all of the structures involved in the complete syndrome are derived.

If the family history of this child is known and there have been no records of cases of fragilitas ossium, the chances are that a 2 year old girl will have no difficulties from the standpoint of pathologic fractures (McGarry, H. H.: Osteopsathyrosis [Fragilitas Ossium], *Canad. M. A. J.* **41**:354 [Oct.] 1939).

PORT WINE NEVUS

To the Editor:—**Would it be right to treat a port wine mark which covers almost half the face and half the body of a newborn infant? What is the best method? The mark is not raised.**

M.D., New York.

ANSWER.—Unfortunately there is no satisfactory method of treating a port wine nevus. In a case of this sort treatment will be without benefit. The stain on the face can be satisfactorily disguised by the skilful application of a protective cosmetic cream such as "Cover Mark." Treatment is apt to make the condition worse by producing scarring. Under no circumstances should radium or roentgen rays be used.

YEASTS IN URINE AND PROSTATE

To the Editor:—**I would like to supplement the remarks in answer to a query in The Journal, Jan. 25,, 1941, page 356, under the heading "Yeasts in Urine and Prostate." My attention was called to this condition in 2 boys in their teens who had other diagnostic combinations but consistently had yeast and molds in both the urine and the prostatic secretion. After scrutiny of the literature and further studies I came to the conclusion that the condition is not as rare in the genitourinary tract as the answer to the query implies. I have found it more frequently in urine from the male bladder than that of women. I do not know why. In the answer to the query it is stated that the "occurrence of yeast in the prostatic secretion is even more rare." This has not been my experience, as I have found yeast in the prostatic secretion of scores of men. The answer recommends irrigations of the bladder; while I find that they are helpful and soothing, at the same time I believe that they are chiefly palliative and that internal medication is also indicated to produce quicker and better results. My observations in the cases described lead me to believe that, while these yeasts and molds are probably saprophytes, at the same time their pathologic and clinical urologic manifestations have always been in connection with some other entity, and therefore the combination is associated in what I term "pathologic symbiosis." I feel that too little research has been done along this line and that too little has appeared in the medical literature. While infection with yeast is probably a dual infection, at the same time the end result manifests itself as an entity hitherto little understood but at the same time a clinical one with distressing, debilitating, tenacious and chronic manifestations. With the advent of the new chemical drugs I felt hopeful that specific cures would result. While in the main they have shown better results than some of the older lines of treatment, I have been disappointed that the percentage of cures has not been larger. I have one little boy who has shown decided improvement with the use of sulfathiazole and to a lesser extent sulfanilamide before this but who relapses after a few months and has repeated recurrences of as great intensity and severity as before. Prior to the use of these modern drugs I used with less success alternating courses of treatment with gradually increasing doses of saturated solution of potassium iodide (at one time considered the best and most reliable drug in these conditions) and 1 grain (0.06 Gm.) doses of methylene blue over periods of several months with rest periods of several months.**

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